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13. Abstract ***(Maximum 200 Words)*** ***(abstract should contain no proprietary or confidential information)***
During the first year of this grant, an extensive retrospective database was constructed with emphasis on early hemodynamic studies of patients with severe trauma. The goal is to produce a comprehensive, objective, unbiased database that can be independently mined by members of the combat-casualty-care community. The database is expected to provide insight into the resuscitative outcome of combat casualties and civilian trauma victims. One of the major goals of this project is to identify physiological parameters that are strong predictors of outcome or reflect the need for further therapy. A total of 689 patients are currently in the main database. These patients were monitored with state-of-the-art non-invasive sensors as well as with invasive techniques and procedures. The database is considered very high in quality and utility because the diagnostic measurements are comprehensive, and the prevalence of non-survivors is high. Approximately 180 additional patient histories were processed during the first project year, which represents an increase of ~40% in the number of trauma patients studied compared to the previous year. Additional data are required for the development of a large validation group to test predictor-guided models. An initial assessment of outcome predictors indicates that a mathematical "nearest neighbor" analysis is the best technique for predicting survival/non-survival, whereas $PtcO_2/FIO_2$ has emerged as the best single parameter predictor. The overall goal is to identify patients who are at risk in the earliest stage of the therapeutic process, adjust therapies to improve outcomes, and promptly determine whether the new therapy will lead to survival. In this regard, analyses of hemodynamic patterns provide an important decision-making aid.

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Table of Contents

1. Introduction

This research program focuses on the resuscitation of traumatic casualties in hypovolemic shock. The principal objectives are to determine:

- when it is necessary for a medic on the battlefield to resuscitate a trauma victim,
- how the effectiveness of the resuscitation effort can be measured objectively with outcome predictors, and
- what is the desired end point of resuscitation: can it be defined empirically by the survivors' values?

Human studies at a major Level I trauma center, Los Angeles County+USC Medical Center (LAC+USCMC), serve to precisely define the pathophysiology of traumatic/hemorrhagic shock and test the effectiveness of noninvasive (or minimally invasive) sensors of tissue perfusion failure. The investigation entails the consolidation of three large existing trauma data sets at LAC+USCMC into a new database containing existing medical record data without the possibility of patient identification. Our use of the term "existing medical record, EMR" data in this report automatically carries the qualifier "without the possibility of patient identification". The current database tracks the trauma victim beginning at the emergency department, then to the operating room, the radiology suite when indicated, and the surgical intensive care unit (SICU). It provides an excellent reference source and testing facility for the current state-of-the-art in U.S. resuscitative medicine. Our goal is to make the entire trauma database accessible to the combat-casualty-care community in an easy-to-use, straightforward fashion. Thus, each member of the community will be able to derive his or her own conclusions from a comprehensive, objective, unbiased database. Taken as a whole, the new database will allow optimum resuscitation strategies to be developed for the Army medic and will serve as a guide for implementing new sensor strategies. The LAC+USCMC data is being "packaged" with a database management program and augmented with a user-friendly, menu-driven program for standard analyses and data manipulation.

2 Body of Report

During this first grant year, particular attention was paid to building the infrastructure for the trauma database and populating the database with EMR patient case histories. In addition, outcome predictors were investigated within the context of a mathematical "nearest neighbor" model as well as in studies involving single parameter predictors.

2.1 Human Hemodynamic Data Processing, Analysis, and Interpretation

Despite the large number of existing trauma cases in the William C. Shoemaker (WCS) database at LAC+USCMC, it became clear in the early stages of this study that more retrospective cases were needed. In part, this is because the sensors and methods of noninvasive hemodynamic data acquisition have improved with time. As a result, the more recent data sets obtained within the past five years are substantially higher in quality than much of the data acquired prior to 1996. (Approximately 1500 trauma cases were documented at hospitals other than LAC+USCMC prior to 1996.) Thus, the recent LAC+USCMC data allows us to address the questions of Section 1 in a more comprehensive fashion. At the same time the latest data has proven very useful in studies of outcome predictors. Both the stochastic prediction methodology [Ref 1] and the search for single parameter predictors yielded significant results with the latest data sets. The acquisition of more data allows the phase space of the mathematical model to be more fully populated and therefore improved. In addition, both areas of inquiry greatly benefit from the existence of a large validation data set. In summary, there is a strong rationale for acquiring more data from existing medical records for inclusion in the trauma database.

During the period September 29, 2001 through September 28, 2002, approximately 180 new trauma cases were added to the WCS database. This is an increase of about 40% compared to the previous year. Funds from the current Army grant were used for the processing, analysis, and interpretation of the 2002 data as well as all other retrospective data acquired between 1996 and 2001. Methods for noninvasive data acquisition are described below, and the results of year 1 efforts to analyze and interpret the WCS database are discussed. This investigation was performed outside the framework of the Main Project Database because the Database was concurrently constructed while the hemodynamic research was being performed. A single-parameter predictor study was initiated after the Database was completed. This is discussed in Section 2.2.8.

2.1.1 General Methods for Noninvasive Hemodynamic Data Acquisition.

At Los Angeles County + USC Medical Center (LAC+USCMC), electrodes are attached to the base of the neck and to the lower lateral chest wall for thoracic electrical impedance measurements of cardiac output, and a finger probe is used for pulse oximetry ($SapO_2$). Also monitored are arterial blood pressure, heart rate, and ECG as general circulatory measures. In addition, physicians evaluate tissue perfusion/oxygenation by transcutaneous oxygen/CO_2 sensors that have the same Clark polarographic oxygen sensor used routinely in the standard blood gas analyzer. While the oxygen tension of heated skin of the chest does not reflect the state of oxygenation of all tissues, it has been shown to be a sensitive early warning of hypovolemic shock [Refs. 1-3]. All parameters are monitored and recorded continuously after emergency department (ED) admission or following the onset of surgical operations. In so far as is possible, LAC+USCMC specifically records these hemodynamic variables before and after each therapy, beginning with admission to the ED, following the patient to the operating room (OR) and intensive care unit (ICU). Each therapeutic intervention is noted in time, dose, duration of infusion, and time after admission. Each therapy is given one-at-a-time, if possible (except for clinical exigencies), with hemodynamic monitoring before, during and after its administration. Perioperatively, noninvasive hemodynamic data in high-risk surgical patients is started in the OR or ICU prior to anesthesia and maintained throughout the operation. Blood losses are estimated by vital signs, hematocrits, urine output, sponge counts, amount of fluid in the suction bottles, number of transfusions needed to maintain normal hematocrit values, and clinical observations. Estimated blood losses are promptly replaced.

2.1.2 Analysis and Interpretation of the Database in Terms of Outcome Prediction

Over the past year, we confirmed that multiple noninvasive monitoring systems are feasible and highly useful methods to acquire early information from patients with acute life-threatening trauma [Ref. 1]. These noninvasively monitored data:

- were sufficiently close to the information supplied by the PA catheter to be a useful surrogate for invasive monitoring;
- could be used immediately after Emergency Department (ED) admission and throughout the hospital (analogous to use in prehospital settings),
- could be used to compare the time course of clinical and hemodynamic parameters;
- provided continuous, real time displays and data streams rather than traditional methods that provide infrequent and intermittent "snapshots";
- were utilized to describe the physiologic and pathologic patterns of patients with severe trauma and other emergencies during resuscitation immediately after admission to the ED;
- revealed hemodynamic patterns of severe trauma that are related to outcome; and
- most importantly, provided information to a user-friendly program that can be used effectively by nurses and other paramedic personnel at the bedside of acutely ill patients.

In addition to the conventional vital signs, hematocrit, urine output, blood gases, and other clinical evaluations, we are currently evaluating noninvasive hemodynamic monitoring used with a new mathematical analysis for application to acute high-risk critical illness, shock, and potentially lethal organ failure beginning with ED admission. To evaluate the accuracy of the random (stochastic) analysis, we are investigating various subsets of trauma including blunt or penetrating injury to chest, abdomen, extremity, head, neck and spinal cord in various combinations.

We plan to employ hemodynamic patterns to develop outcome predictors using the new mathematical analysis and data mining programs to elucidate underlying hemodynamic deficiencies, to evaluate and compare the effectiveness of various therapies in previously recorded databases, and to display possible optimal therapy in a real-time mode for each new individual patient at each stage of the patient's hospital course. In addition we plan to utilize additional tools to evaluate their concordance with established patterns of monitored data and physiologic patterns. Therapeutic policies based on analyses of the databases, along with outcomes of other competing therapeutic and diagnostic modalities, are also being investigated [Refs. 2-4].

As shown in Table 1, we have found markedly different misclassification rates in the same series of trauma patients from single isolated values of vital signs, cardiac index, APACHE II, discriminant analysis, and now by using the present version of the stochastic analysis program. Heart rate, mean arterial pressure (MAP), and cardiac index values were the initial or lowest values as stated, APACHE II values were calculated on a daily basis, discriminant analysis covered the resuscitation period, and the probability analysis was calculated for each set of values; the first set of values are presented here. The data show the limitations of these single values. By contrast, there are advantages of a computerized database of multiple noninvasive variables organized over time.

Table 1 Misclassifications in Outcome Prediction by Evidence-based Analyses

Method	Criteria	Misclassification Rate
Initial Heart Rate	**S <95, NS>96 beat/min**	**(70/159) 45%**
Initial MAP	**S >85, NS<70 mmHg**	**(76/159) 47%**
Lowest MAP	**S >50, NS< 50 mmHg**	**(83/159) 52%**
Initial Cardiac index	**S>3.8, NS< 3.8 L/min/m2**	**(72/159) 43%**
APACHE II	**S <27, NS >27**	**(30/97) 31%**
Discriminant Analysis	**(See Ref. 22)**	**(23/151) 15.2%**
Probability Analysis,	**S>75%, NS <55%**	**(16/165) 9.2%**

Initial studies showed over 90% accuracy in predicting outcome in the first 12 hours after ED admission using the new mathematical (nearest neighbor) analysis and display program that estimates the probabilities of survival based on the primary diagnosis, selected relevant covariates, and noninvasive hemodynamic monitoring of cardiac, respiratory, and tissue perfusion functions. We plan to study approximately 150 severe high-risk patients during the coming year. They are drawn from a pool of over 5000-trauma admissions/year to our Trauma/Critical Care Service. We plan to continue our study of the most severely ill of these trauma patients.

The monitoring and information system also displays a decision support system to provide the physician at the bedside with a potentially useful method for optimizing the therapy by evaluating each potential therapy based on responses of the nearest neighbors in terms of reduced mortality. The system may be used to diagnose, evaluate, and suggest therapy for the early hemodynamic aspects of circulatory dysfunction, shock, and critical illness anywhere in the hospital including the ED, operating room, post

anesthesia recovery room, intensive care unit (ICU), step-down units, hospital floors, pre-hospital areas, and outpatient clinics. The major underlying challenge is to develop an information system based on a sufficiently large noninvasive database with adequate numbers of nearest neighbors to predict outcome. Ultimately this data base will support a therapeutic decision support system that will display the effects of therapies that had been given to similar patients (nearest neighbors), and identify the therapies that carry the greatest expectation of optimizing survival. Since the computational burden does not appear to be intense, the system was designed to function in a real-time mode at the bedside. Alternative therapies and the probability for reduced severity (mortality) will be displayed at each stage of acute life-threatening illness as well as before and after each therapy. These data along with all supporting evidence will provide the physician with maximal information for selecting therapies to optimize outcome. The quest for early diagnosis and therapy of circulatory shock is analogous to that of cancer, where early therapy is far more effective and less costly. In fact the concept of the "Golden Hour", the major descriptor of the response to trauma, is largely based on the need to provide therapy in the earliest stage of traumatic injury. In preliminary studies on a consecutively monitored group of severely traumatized patients with 30% mortality, the stochastic analysis program correctly identified survivors and nonsurvivors with over 90% accuracy in the first 12 to 24 hours after admission. There were 16/165 patients or 9.7% who were misclassified in this initial resuscitation period [Ref. 3]. Inspection of the data revealed that accuracy might be limited by the number of patients that comprised the pool of nearest neighbors for each etiologic category in the database. We will address this problem by increasing the number of trauma subsets and other diagnostic categories studied.

2.2 Development of the Trauma Database With Emphasis on Hemodynamics Including Blood Flow and Adequacy of Tissue Perfusion

As part of this project, we are assembling a large trauma database using data gathered at Los Angeles County + USC Medical Center (LAC+USCMC), with the capacity for additional data integration from other sources. The goal is to produce a comprehensive, objective, unbiased database that can be independently mined by members of the combat-casualty-care community. The database is expected to provide insight into the resuscitative outcome of combat casualties and civilian trauma victims. One of the major goals of this project is to identify physiological parameters that are strong predictors of outcome or reflect the need for further therapy.

Our original statement of work indicated that there were only two databases that needed to be combined as part of this project. These were the William C. Shoemaker (WCS) database and the SICU database. However, it quickly became apparent that the benefits of including a third database, the trauma registry (TR), were very large. The TR contains the official LAC+USCMC summary of each trauma case and includes admission and discharge data. (See Table 8 for a partial parameter list.) Its role is to improve the efficiency of the trauma care system [Ref. 5]. TR records at LAC+USCMC are collected into a relational database that is amenable to computer processing. As a result, The Main Project Database currently consists of three dissimilar elements: the WCS database, the SICU database, and the TR. The WCS database tracks patients using predominantly non-invasive measures beginning with resuscitation in the emergency department (ED) through the RAD/OR and into the SICU. Patient histories terminate at discharge or death. Approximately 20-30 physiological parameters are recorded for ~689 individual patients from 1996 to present. Most measurements are non-invasive and the quality of these data is very high. The catalog of WCS parameters has evolved because of the introduction of new non-invasive sensors. However, the database is anchored by a set of common parameters. The massive SICU database provides a comprehensive electronic record of all customary diagnostic measurements, procedures, and therapies. Many are invasive in nature, and most are considered "gold standard" measurements. Supplemental data is supplied by the TR, including information obtained by

paramedics and ED personnel. The tools being developed to probe the database are flexible and are not limited to specific methodologies or techniques.

2.2.1 Database Assembly

As noted above, the database constructed as part of this project serves as a tool for assessing a variety of interventions and is expected to provide insight into the resuscitative outcome of combat casualties and civilian trauma victims. One of the major goals of this project is to identify physiological parameters that are strong predictors of outcome or reflect the need for further or modification of therapy. At this point, we don't know whether or not a sensor system can fully replace a medic's judgment. It is most likely that new sensors or arrays of sensors will be identified that can enhance the ability of the medic or other responder to asses the status of a casualty. Some predictors may require a combination of sensor readings and a medic's judgement. Other questions related to the most desirable beginning and end points of the resuscitation process and what therapies produce the most survivors can be explored with the existing database. Overall, the data mining process is quite general and is not restricted to any single methodology. Many distinct mining strategies are expected to evolve with time.

2.2.2 The "Toy Database"

During the current grant year, a test data set referred to as the "toy database" was initially constructed. It consists of small portions of the William C. Shoemaker (WCS) database, the SICU database, and the LAC+USCMC trauma registry (TR). The toy database was assembled to test the practicability of combining the three diverse databases. In the case of the SICU database, the number of extracted parameters was limited to ~30. Approximately 24 parameters were extracted from the TR, and all data from the WCS Heart Rate Variability (HRV) study (discussed below) were included. The WCS database takes the form of entries in Microsoft Excel spreadsheets. Both the SICU and TR databases are relational in nature and are hosted by two different database programs, Sybase (SICU) and Foxbase (TR), respectively. The objective behind assembling the toy database was to identify problems involved in the consolidation of these three data sets. The ICU database is by far the largest; it is 50 to 100 times larger than the WCS database. The TR is in itself a very large database, but the amount of data/information that is extracted for individual trauma patients is approximately equal to the corresponding patient file sizes in the WCS database. Data dictionaries had to be developed for all three data sets because they had never been used outside of their targeted application. Figure 1 below illustrates the intersection of the three databases; the area with the star represents the data records that became part of the toy database. A total of 53 patient histories were common to all three data sets (WCS, SICU, and the TR). These were merged together into a single database using the Sybase Anywhere 8.0 database program. A listing of toy database parameters is provided in the Table 2 below. This new test database was probed and queried primarily with SQL commands to verify that it was properly ordered and complete.

It was found that a considerable effort is involved in sorting and bringing large quantities of diverse data from the SICU database into the main Sybase database. In addition, there is a strong preference for data obtained at the earliest times following patient admission at LAC+USCMC. The SICU data typically begins 6 to 24 hours after admission, whereas the WCS data typically begins at admission. As a result, our initial efforts focused on merging the WCS database and the TR database into a single project database. This allowed the early time hemodynamics of trauma patients to be examined in detail during the first grant year. At the request of the Government, all relevant comments (i.e. character strings) in the WCS data sets were parsed so that they could be readily interpreted as part of the Main Project Database. This was a significant task involving the parsing of more than 50,000 comments. This task required two and a half months to complete.

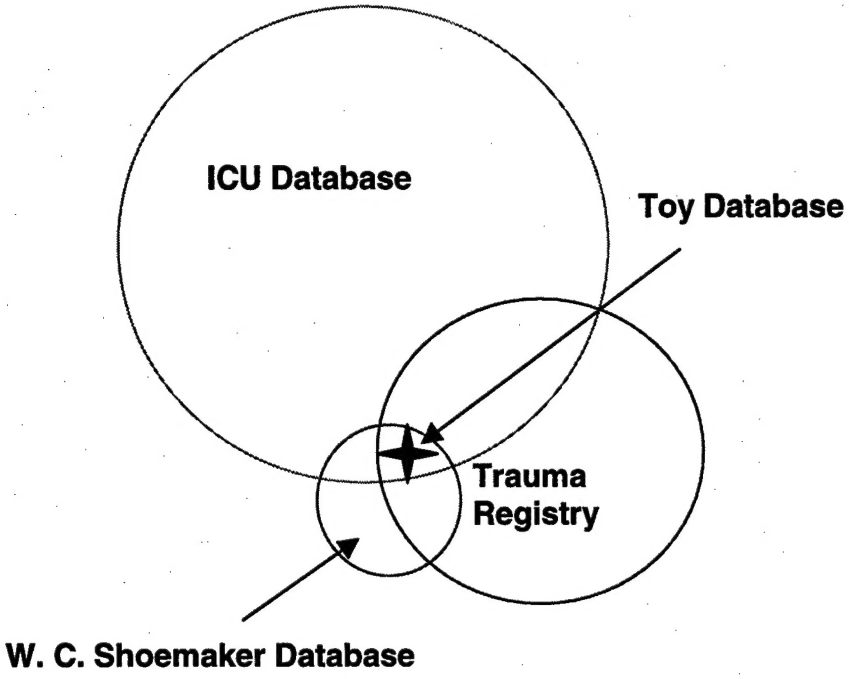

Figure 1. Data for the Toy Database was extracted from the intersection of three large data sets.

Table 2. Parameters Used in the Toy Database

Table: HRV_COTD – HRV Data (WCS)

Column Name	*Format*	*Description*
dt	Timestamp	Date/Time of measurement
hrv_psn	tinyint	Pt number from HRV study
hrv_evt	integer	Event number from HRV study
cotd	numeric(4,2)	Cardiac Output (Thermodilution) value

Table: HRV_FRQ – HRV Data (WCS)

Column Name	*Format*	*Description*
dt	Timestamp	Date/Time of measurement
hrv_psn	tinyint	Pt number from HRV study
hrv_evt	integer	Event number from HRV study
lfa	double	Low Frequency Area
rfa	double	Respiratory Frequency Area
fract	double	LFA/RFA
mhr	double	mean HR

Table: HRV_INTEG – HRV Data (**WCS**)

Column Name	***Format***	***Description***
dt	Timestamp	Date/Time of measurement
hrv_psn	tinyint	Pt number from HRV study
hrv_evt	integer	Event number from HRV study
q_admit_dt	timestamp	Admission Date/Time
T	double	Time since admission, in hours & decimal fraction

Table: HRV_OXY1 – HRV Data (**WCS**)

Column Name	***Format***	***Description***
dt	Timestamp	Date/Time of measurement
hrv_psn	tinyint	Pt number from HRV study
hrv_evt	integer	Event number from HRV study
pao2	integer	PaO_2
saow	integer	SaO_2
hct	numeric(4,2)	Hematocrit

Table: HRV_OXY2 – HRV Data (**WCS**)

Column Name	***Format***	***Description***
dt	Timestamp	Date/Time of measurement
hrv_psn	tinyint	Pt number from HRV study
hrv_evt	integer	Event number from HRV study
svo2	integer	SVO_2
o2_delivered	integer	O_2 Delivered
o2_consumed	integer	O_2 Consumed
dt	Timestamp	Date/Time of measurement
hrv_psn	tinyint	Pt number from HRV study
hrv_evt	integer	Event number from HRV study
cobi	integer	Cardiac Output Bioimpedance
cibi	double	Cardiac Index Bioimpedance
hr_ekg	numeric(4,1)	HR from EKG
map	integer	Mean Arterial Pressure
ptc_O2	integer	ptco2
ptc_CO2	integer	ptcco2
FIO2	double	FIO2
ptcO2_FIO2	double	ptco2/FIO2
sapO2	integer	sapo2

Table: HRV_PT_LIST – HRV Data (**WCS**)

Column Name	***Format***	***Description***
PSN	numeric(7,0)	Patient Study Number (assigned for this study)
HRV_PSN	tinyint	Patient number from HRV study
PF	double	Hospital assigned PF number
SURVIVED	bit	1 = pt survived, 0 = pt died
AGE	tinyint	Age in years
MALE	bit	1 = male, 0 = female

Column Name	*Format*	*Description*
HEIGHT	tinyint	Height
WEIGHT	smallint	Weight
DX	varchar(255)	Diagnosis & notes
ADMIT_DT	timestamp	Date/Time of admission
OPERATE_DT	timestamp	Date/Time of operation (if any)
DISCHARGE_DT	timestamp	Date/Time of discharge
BLOOD_LOSS_EST	smallint	Blood Loss Estimate
COMPLICATION	varchar(255)	Notes about complications
ARDS_DATE	timestamp	Date/Time of ARDS, if any
BSA	numeric(2,1)	???
SCORE_GCS	tinyint	GCS score
Location	varchar(40)	Patient location
Notes	varchar(40)	Notes

Table: HRV_PT_LOCATION – HRV Data (**WCS**)

Column Name	*Format*	*Description*
dt	timestamp	Date/Time
hrv_psn	tinyint	Pt number from HRV study
Location	varchar(8)	Pt location

Table: icu_bp2 – SICU Data (**SICU**)

Column Name	*Format*	*Description*
emtek_id	integer	SICU ID number
obj	varchar(12)	BP source (ART or BP)
dia	numeric(5,2)	Diastolic BP
sys	numeric(5,2)	Systolic BP
mean	numeric(5,2)	Mean Arterial Pressure
dt	timestamp	Date/Time of measurement

Table: icu_cardiac – SICU Data (**SICU**)

Column Name	*Format*	*Description*
emtek_id	integer	SICU ID number
svri	numeric(5,1)	Systemic Vascular Resistance, Indexed
svr	numeric(6,2)	Systemic Vascular Resisitance
co	numeric(5,2)	Cardiac Output
ci	numeric(5,2)	Cardiac Index
dt	timestamp	Date/Time of measurement

Table: icu_demo – SICU Data (**SICU**)

Column Name	*Format*	*Description*
PSN	numeric(7,0)	Patient Study Number (assigned for this study)
HRV_PSN	tinyint	Patient number from HRV study
PF	numeric(8,0)	Hospital assigned PF number
emtek_id	integer	SICU ID number
admit_dt	timestamp	Admission Date/Time

Column Name	*Format*	*Description*
icu_dt	timestamp	SICU Admission Date/Time
ageadm	smallint	Age at admission
bdate	datetime	Date of Birth
weight	numeric(5,2)	Weight
height	numeric(5,2)	Height
gender	char(1)	Male = 'M', Female = 'F'
survived	char(1)	Yes = 'Y', No = 'N'

Table: icu_fluids – SICU Data **(SICU)**

Column Name	*Format*	*Description*
emtek_id	integer	SICU ID number
v_in	numeric(8,1)	Fluids in for day
v_out	numeric(8,1)	Fluids out for day
v_net	numeric(9,1)	Net fluids for day
dt_day	date	Date for measurement

Table: icu_hr – SICU Data **(SICU)**

Column Name	*Format*	*Description*
emtek_id	integer	SICU ID number
hr	numeric(5,2)	Heart Rate
dt	timestamp	Date/Time of measurement

Table: icu_labs – SICU Data **(SICU)**

Column Name	*Format*	*Description*
emtek_id	integer	SICU ID number
object	varchar(12)	Lab test abbreviation
value	flloat	Lab results
dt	timestamp	Date/Time of measurement

Table: icu_rr – SICU Data **(SICU)**

Column Name	*Format*	*Description*
emtek_id	integer	SICU ID number
rr	numeric(5,2)	Respiration Rate
dt	timestamp	Date/Time of measurement

Table: icu_tempr – SICU Data **(SICU)**

Column Name	*Format*	*Description*
emtek_id	integer	SICU ID number
tempr	numeric(3,1)	Temperature (degrees C)
dt	timestamp	Date/Time of measurement

Table:toy_psn **(WCS, SICU, TR)**

Column Name	*Format*	*Description*
psn	smallint	Patient Study Number for this study
pf	numeric(7,0)	Hospital assigned PF number

Column Name	*Format*	*Description*
hrv	tinyint	HRV study patient number
tr	numeric(10,0)	Trauma Registry pt acct number
icu	integer	ICU emtek_id pt number

Table: tr_demo– TR Data **(TR)**

Column Name	*Format*	*Description*
PSN	numeric(7,0)	Patient Study Number for this study
PF	numeric(7,0)	Hospital assigned PF number
HRV_PSN	tinyint	HRV study patient number
acctno	decimal(20,5)	Trauma Registry pt acct number
emtek_id	integer	CU emtek_id pt number
er_enter_dt	timestamp	Date/Time ER entry
er_exit_dt	timestamp	Date/Time ER exit
er_los_calc	numeric(6,2)	er_exit_dt – er_enter_dt in hours
er_los_rec	numeric(5,2)	ER length of stay as recorded in TR
IV_FLUIDS	numeric(5,1)	Total IV Fluids from ER
Penetrating	varchar(1)	Penetrating = P, Blunt = B
surg_hrs_dt	numeric(15,2)	Hours from ER admit to surgery
iss	tinyint	ISS
ais_1_head	tinyint	AIS Head Score
ais_2_head	tinyint	AIS Face Score
ais_3_head	tinyint	AIS Chest Score
ais_4_head	tinyint	AIS Abdomen Score
ais_5_head	tinyint	AIS Extremeties Score
ais_6_head	tinyint	AIS External Score
sbp	numeric(5,1)	Systolic BP
dbp	numeric(5,1)	Diastolic BP
mbp	numeric(5,1)	Mean BP
Age	numeric(5,2)	Age
Sex	char(1)	M/F
Weight	numeric(5,2)	Weight (kg)
Survived	char(1)	Y/N

2.2.3 Main Project Database

The Main Project Database contains existing medical record (EMR) data and currently consists of 689 trauma patients from the WCS data sets and corresponding patient data from the TR. As of September 28, 2002, the SICU database has been sorted and pre-processed for inclusion in the Main Database but had not yet been formally included. The patients studied were monitored with state-of-the-art non-invasive sensors as well as with invasive techniques and procedures. Overall, the Database is considered to be very high in quality and useful in prediction because the diagnostic measurements are comprehensive, and the prevalence of non-survivors is high. The Main Project Database includes temporal records of medications, blood component therapies, resuscitation fluids, and procedures. In addition, the location of the patient in the hospital is provided as a function of time. The temporal point of reference in the Database is the time of admission.

Both the WCS and TR database involve significant numbers of keyed entries without the benefit of a supervising program to prevent unintended characters/values from entering the database. A Visual Basic program was written to examine each cell of the WCS Excel sheet for correctness of data format and to determine whether data values were in range. This procedure helped identify errors and made the transformation of the Excel Sheets to database tables easier. Ultimately, SQL queries of the data sets within the Sybase program were used to determine whether unreasonable or inconsistent information was contained in the WCS and TR data sets. In the case of the WCS data set, the records of W. C. Shoemaker were used to verify the data, whereas archived patient charts were examined to correct the TR. Correcting the TR is a time consuming endeavor.

In Table 3, we characterize the data from the WCS and TR data sets that currently reside in the Main Project Database. The WCS data are organized into several individual data sets. These datasets have been used in several focused studies conducted in the past at LAC+USCMC [e.g., Refs. 6-11]. The percentage of patients covered by various physiological parameters is presented in Table 3 to help characterize the sensor coverage. Abbreviated notations for the physiological variables are used in the tables below; detailed definitions of the parameters are provided at the end of this subsection (pages 21-25).

Table 4 summarizes EMR patient data processed in 2002. These results require that the TR be updated by hospital personnel before the new data can be fully incorporated into the Main Project Database. The TR updates typically lag the WCS data acquisition by ~6-12 months. During the current grant year, approximately 180 new EMR patient histories were processed, which represents an increase of ~40% in the number of trauma patients studied compared to the previous year. At present, the outcomes of some of the patients in the Surgical ICU 5 data set are not known, and as a result the exact number of non-survivors is not known.

A summary of physiological parameters versus WCS data set is provided in Table 5 along with the percentage of patients covered by each measurement. The first 17 parameters in the table have become standard quantities within the WCS database for assessing blood flow and tissue perfusion. Several other non-invasive parameters are associated with the heart rate variability study. The standard non-invasive diagnostics of hemodynamics include electrical bioimpedance measurements of cardiac output, pulse oximetry, and transcutaneous measurements of oxygen and carbon dioxide tension. A brief description of the each these diagnostics is provided below; greater detail may found in Refs. 6 and 12. The Heart Rate Variability Protocol and the Surgical ICU 2, 3, and 4 studies made use of a special purpose instrument that measures heart rate variability parameters (ANS-R1000, Ansar Inc., Philadelphia, PA). This unit yields values for L(mean), R(mean), L/R(mean), and HR(mean) shown in Table 5.

Bioimpedance Measurements. A thoracic bioelectric impedance device (Yantagh, Inc., Bristol, PA) is usually applied shortly after arrival of the patient in the emergency department. Noninvasive disposable pre-wired hydrogen electrodes are positioned on the skin, and three EKG leads are placed across the precordium and left shoulder. A 100 kHz, 4 mA alternating current is passed through the patient's thorax by the outer pairs of electrodes. The voltage is sensed by the inner pairs of electrodes, which capture the baseline impedance (Z_0), the first derivative of the impedance waveform (dZ/dt), and the EKG. The EKG and bioimpedance signals are filtered with an all-integer-coefficient technology to decrease computation and signal processing time. The signal processing algorithm uses a time-

Table 3. W. C. Shoemaker Data Currently in the Main Database

Study Name: Fluid Resuscitation Protocol
Focus: Effectiveness of resuscitative fluids on tissue perfusion.
Number of Patients: 333, 78 non-survivors, 23.4% non-survivors
Earliest Admission Date: 7/27/96 (patient 1)
Last Admission Date: 3/25/99 (patient 333)
Recorded Parameters and Percentage of Patients Covered by Measurement

CItd	CIbi	HR	MAP	SapO2	PtcO2	PtcCO2	FIO2	SaO2
25.2	95.8	95.8	94.3	94.0	92.8	92.8	94.9	59.2
SvO2	HCT	DO2I	VO2I					
16.5	60.7	59.5	16.5					

Study Name: Heart Rate Variability Protocol
Focus: Non-invasive measurements of autonomic nervous system. Heart rate variability and respirator activity.
Number of Patients: 179, 43 non-survivors, 24.0% non-survivors
Earliest Admission Date: 8/18/99 (patient 2)
Last Admission Date: 10/14/00 (patient 179)
Recorded Parameters and Percentage of Patients Covered by Measurement

COtd	COrb	STAR	CObi	CIbi	HR	MAP	PtcO2		
56.4	20.7	20.7	91.1	91.1	96.6	96.6	91.6		
PtcCO2	FIO2	tcO2/F	SapO2	L(mean)	R(mean)	L/R(mean)	HR(mean)	PaO2	SaO2
91.6	96.6	91.6	96.6	97.8	98.9	99.4	100.0	77.7	77.7
SvO2	HCT	DO2I	VO2I	Qs/Qt					
46.4	77.7	49.2	45.3	43.0					

Study Name: Surgical ICU 2
Focus: Comparison of invasive and non-invasive measurements on a periodic basis.
Number of Patients: 67, 16 non-survivors, 23.9% non-survivors
Earliest Admission Date: 8/9/00 (patient 16)
Last Admission Date: 5/31/01 (patient 67)
Recorded Parameters and Percentage of Patients Covered by Measurement

COtd	COrb	VCO2	ETCO2	Pox	STAR	TV	RR		
67.2	25.4	25.4	25.4	25.4	25.4	55.2	40.3		
CObi	CIbi	Zo	dZdT	HR	MAP	PtcO2	PtcCO2	FIO2	
98.5	98.5	3.0	4.5	100.0	100.0	92.5	92.5	100.0	
tcO2/F	SapO2	L(mean)	R(mean)	L/R(mean)	HR(mean)	PaO2	SaO2	SvO2	HCT
100.0	98.5	11.9	11.9	11.9	4.5	76.1	76.1	52.2	76.6
DO2I	VO2I	Qs/ Qt	BE	PEEP	CVP				
55.2	52.2	52.2	56.7	50.7	38.8				

Study Name: Surgical ICU 3
Focus: Comparison of invasive and non-invasive measurements on a periodic basis.
Number of Patients: 108, 21 non-survivors, 19.4% non-survivors
Earliest Admission Date: 3/11/01 (patient 1)
Last Admission Date: 11/24/01 (patient 108)
Recorded Parameters and Percentage of Patients Covered by Measurement

CIbi	HR	MAP	SapO2	tcO2/F	CiId	COrb	FIO2	PaO2 82.4	SaO2
99.1	100.0	100.0	100.0	100.0	46.3	4.6	100.0		82.4
SvO2	HCT	DO2I	VO2I	Qs/Qt	BE	L(mean)	R(mean)	L/R(mean)	PtcCO2
49.1	83.3	50.0	50.9	50.0	80.6	17.6	17.6	17.6	100.0

Table 4. W. C. Shoemaker Data Processed in Calendar Year 2002

(EMR patient data processed in 2002 require that the TR be updated before the new results can be fully incorporated into the Main Project Database.)

Study Name: Surgical ICU 4
Focus: Comparison of invasive and non-invasive measurements on a periodic basis.
Number of Patients: 110, 28 non-survivors, 25.5% non-survivors (Preliminary)
Earliest Admission Date: 11/26/01 (patient 1)
Last Admission Date: 7/22/02 (patient 110)
Recorded Parameters and Percentage of Patients Covered by Measurement

CIbi	HR	MAP	SapO2	PtcCO2	tcO2/F	CItd	FIO2	PaO2	SaO2
100.0	100.0	100.0	99.1	95.5	100.0	47.3	100.0	79.1	79.1
SvO2	HCT	DO2I	VO2I	Qs/Qt	BE	L(mean)	R(mean)	L/R(mean)	
51.8	80.0	50.9	49.1	49.1	75.5	4.5	4.5	4.5	

Study Name: Surgical ICU 5 (in Progress)
Focus: Comparison of invasive and non-invasive measurements on a periodic basis.
Number of Patients: 55, at least 9 non-survivors. The exact number of non-survivors cannot be determined as of 10/09/02. The final status of 10 patients is not known at present.
Earliest Admission Date: 7/21/02 (patient 1)
Lastest Admission Date: 9/28/02 (patient 55).
Recorded Parameters and Percentage of Patients Covered by Measurement

CIbi	HR	MAP	SapO2	PtcCO2	tcO2/F	CItd	FIO2	PaO2	SaO2
100.0	100.0	100.0	100.0	100.0	100.0	36.7	100.0	73.3	73.3
SvO2	HCT	DO2I	VO2I	Qs/Qt	BE	L(mean)	R(mean)	L/R(mean)	
40.0	73.3	40.0	40.0	40.0	70.0	0.0	0.0	0.0	

Table 5. Summary of WCS Physiological Parameters Versus Data Set and the Percentage of Patients Covered by Each Measurement

Parameter	Fluid Resus. Protocol 07/96 - 03/99	Heart Rate Variability Protocol 08/99 - 10/00	Surgical ICU 2 08/00 - 05/01	Surgical ICU 3 03/01 - 11/01	Surgical ICU 4 11/01 - 07/02	Surgical ICU 5 07/02 - 09/02 (In Progress)
CItd	25.2	56.4	67.2	46.3	47.3	36.7
CIbi	95.8	91.1	98.5	99.1	100.0	100.0
HR	95.8	96.6	100.0	100.0	100.0	100.0
MAP	94.3	96.6	100.0	100.0	100.0	100.0
SapO2	94.0	96.6	98.5	100.0	99.1	100.0
PtcO2	92.8	91.6	92.5	100.0	100.0	100.0
PtcCO2	92.8	91.6	92.5	100.0	95.5	100.0
FIO2	94.9	96.6	100.0	100.0	100.0	100.0
SaO2	59.2	77.7	76.1	82.4	79.1	73.3
SvO2	16.5	46.4	52.2	49.1	51.8	40.0
HCT	60.7	77.7	76.6	83.3	80.0	73.3
DO2I	59.5	49.2	55.2	50.0	50.9	40.0
VO2I	16.5	45.3	52.2	50.9	49.1	40.0
tcO2/F	92.8	91.6	100.0	100.0	100.0	100.0
PaO2		77.7	76.1	82.4	79.1	73.3
Qs/Qt		43.0	52.2	50.0	49.1	40.0
BE			56.7	80.6	75.5	70.0
COrb		20.7	25.4	4.6		
STAR		20.7	25.4			
CObi		91.1	98.5			
L(mean)		97.8	11.9	17.6	4.5	
R(mean)		98.9	11.9	17.6	4.5	
L/R(mean)		99.4	11.9	17.6	4.5	
HR(mean)		100.0	4.5			
VCO2			25.4			
ETCO2			25.4			
Pox			25.4			
TV			55.2			
RR			40.3			
Zo			3.0			
dZdT			4.5			
PEEP			50.7			
CVP			38.8			

frequency distribution (modified Wigner Distribution) analysis that increases the signal-to-noise ratio. Previous studies have documented satisfactory correlation between thermodilution and bioimpedance cardiac output values in trauma patients [Ref. 13].

Pulse Oximetry. Routine pulse oximetry (Nellcor, Pleasanton, CA) is used to continuously assess arterial oxygen saturation ($SapO_2$). Values are observed and recorded at the exact time of cardiac index measurements. Appreciable or sudden changes in these values are noted and confirmed by *in vitro* arterial oxygen saturation obtained via standard blood gas analysis [Ref. 13].

Transcutaneous oxygen and carbon dioxide tensions. Standard transcutaneous oxygen tension ($PtcPO_2$) measurements (Novametrix Medical Systems, Inc; Wallingford, CT) are made continuously throughout the observation period. Values are noted and recorded at the exact times of cardiac output measurements. The measurement system uses the same Clark polarographic oxygen electrode routinely used in standard blood gas analyses. The oxygen tensions are determined in a representative area of the skin surface heated to 44 C to increase diffusion of oxygen across the stratum corneum and to avoid vasoconstriction in the local area of the skin being measured.

Previous studies demonstrated the capacity of $PtcO_2$ to mirror tissue oxygen tension [Ref. 14]. $PtcO_2$ has been shown to reflect the delivery of oxygen to the local area of skin; it also parallels the mixed venous oxygen tension except under late or terminal conditions where peripheral shunting leads to high mixed venous hemoglobin saturation values [Ref. 14]. Although oxygen tension of a segment of the skin does not replicate the state of oxygenation of all tissues and organs, it has the advantage of being the most sensitive early warning tissue of the adrenomedullary stress response and the adequacy of oxygen delivery to the tissue. Vasoconstriction of the skin is an early stress response to hypovolemia and other shock syndromes.

Transcutaneous CO2 ($PtcCO_2$) monitoring of the skin surface is performed with the standard Stowe-Severinghaus electrode ((Novametrix Medical Systems, Inc; Wallingford, CT).

Heart rate variability measurements. Heart rate (HR) variability and respiratory rate (RR) variability are measured by spectral analysis techniques with the ANS-R1000 instrument. These parameters are indicative of autonomic nervous activity. The spectral areas of variability are divided into low frequency areas, L(mean), and high frequency areas, R(mean). The L(mean) area extends from 0.04 to 0.10 Hz. This area reflects primarily the tone of the sympathetic nervous system as mediated by the cardiac nerve. R(mean), also referred to as the respiratory area, corresponds to a 0.12 Hz-wide frequency interval centered on the fundamental respiratory frequency. It is indicative of vagal outflow reflecting parasympathetic nervous system activity. The L/R ratio reflects the balance between the sympathetic and parasympathetic nervous systems. A recent study [Ref. 8] indicates that a consistently positive relationship exists between HR variability and L(mean) during sudden surges in autonomic activity. This relationship holds to a lesser degree with R(mean). Heart rate variability that reflects autonomic activity is associated with increased MAP, CI, and HR, but decreased tissue perfusion as indicated by the $PtcO_2/FIO_2$ ratio.

The decrease in the heart rate variability data in the year 2002 (Surgical ICU 4 and 5 data sets) is due to the fact that the ANS-R1000 instrument is currently undergoing hardware and firmware upgrades at Ansar Inc. The future role of this instrument in WCS studies has yet to be determined.

Table 6 lists medications, blood component therapies, resuscitation fluids, and procedures included in the WCS database. Patient location versus time can also be determined with the WCS database. Possible patient locations at LAC+USCMC are presented in Table 7 below. Finally, the TR database parameters selected for use in the Main Project Database are listed in Table 8. As noted earlier, these parameters provide an important complement to the WCS and SICU databases.

Table 6. Listing of Medications, Blood Component Therapies, Resuscitation Fluids, and Procedures in the W. C. Shoemaker Data Sets

Medications	Blood Component Therapies and Resuscitation Fluids	Procedures
DOP (Dopamine)	RBC (Packed Red Blood Cells)	Intubation
DOB (Dobutamine)	Plates (Platelets)	Entabation
Morphine	Cryo (Cryoprecipitated Anti-hemophilic Factor)	Dialysis
NaHCO3	WBC (White Blood Cells)	Surgery (start/closing/end times)
Nitroprusside	**Colloids**	CPR
T4 (Thyroxine)	FFP (Fresh Frozen Plasma)	CT
Nitroglycerin	5%/25% Albumin	X-Ray
Lasix	Hespan	Swan-Ganz Catheter Insertion
Atropine	**Crystalloids**	bagging for respirator
25% Mannitol	Normal Saline	Chest tube insertion
Pentobarbiturate	Lactated Ringer's Solution	Angio (Angiography)
		Suction

Table 7. The Location of Patients Versus Time is Included in the W. C. Shoemaker Data Sets

Locations
Emergency Department (ED)
Operating Room (OR)
Radiology
Surgical Intensive Care Unit (SICU)
Continuously Monitored Area (CMA) → Step-Down ICU
Ward

Table 8. Items from the Trauma Registry that are in the Main Database

- Injury Date
- Injury Time
- Mechanism of Injury Description
- Blunt/Penetrating
- Field GCS
- Field Airway Type
- Initial Vital Signs
  - Time
  - BP
  - RR
  - Assisted? Y/N
  - HR
  - Temp
  - Weight
- GCS
  - Eye
  - Motor
  - Verbal
- Labs/Xray
  - C-Spine
  - CT Head
  - CXR
  - Pelvis
  - Ultra Sound
  - CT Abdomen
  - CT Spine
  - Facial Series
  - Other
  - HCT
  - ETOH
  - Toxicology Serum
  - Toxicology Urine
- Procedure
  - ETT/CRIC/Trach
  - ED Thoracotomy
  - DPL (Peritoneal Lavage)
  - Chest Tube: Lt/Rt
  - CPR Duration
- IV Fluids
  - Pre-hospital
  - ED IV Fluids
  - Blood Products
  - Autotrans
- Abbreviated Injury Scale (AIS)
  - (1=Head, 2=Face, 3=Chest, 4=Abdomen, Pelvis, 5=Extremities, 6=External (e.g., skin))
- Blood (Total blood/products received during hospital stay, including Emergency Department)
  - Blood/Products
  - Autotransfuser
  - Total
- Discharge
  - Discharge Date
  - Discharge Time
  - Prior Phase
  - Lived/Died
  - Organ Donation Y/N
  - Discharge to:
    - Home
    - Other Hospital
    - Trauma Center
    - Burn Center
    - Rehab Center
    - Skilled Nursing Facility
    - Morgue
    - Jail
    - AMA (Patient departed Against Medical Advice)
    - Other
- Discharge Diagnoses
- Complications (Y/N)
  - ARDS
  - Cardiac Arrest
  - Colonic Anastomotic Leak
  - Deep Vein Thrombosis (DVT)
  - DVT Lower Extremity
  - Disseminated Intravascular Coagulation (DIC)
  - Empyema
  - Intra-abdominal abscess
  - Jaundice or Hepatic Failure
  - Pancreatic Fistula
  - Pneumonia
  - Pulmonary Embolus (PE)
  - Renal Failure
  - Septicemia
  - Surgical Dehiscence/Evisceration
  - Surgical Wound Infection
  - None
  - Other

Definitions of Physiological Parameters in the W. C. Shoemaker Data Sets

BE

Base Excess
Blood Gas Lab results
(dimensionless, pH)

CIBI

Cardiac Index Bio Impedance
IQ machine
l/min/m^2
Integration is 12 beats

CITD

Cardiac Index measured by Thermodilution
Pulmonary Artery Catheter
l /min / m^2
5 minutes measurement time

COBI

Cardiac Output Bio Impedance
IQ machine
l/min
Integration is 12 beats

COrb

Cardiac Output measured by CO2 Rebreathing
Non-Invasive Cardiac Output (NICO)
l/min

COtd

Cardiac Output measured by Thermodilution
Swan-Ganz TD Catheter
l/min
~ 5 minutes integration time

CVP

Central Venous Pressure
Central Venous Line – average pressure from central line
mm Hg
~ 5 - 10 minutes integration time

DO2I

Oxygen Delivery Index
Calculated from non-invasive systems, ICU computer
ml/minute/m^2
15 minutes measurement time

dZdt

change in baseline
IQ machine
Ohms/sec
12 - 15 beat average

ETCO2

End Tidal CO2
NICO
Torr
~ 1 minute integration time

FIO2

Fractional Inspired Oxygen Concentration
Respirator
Fraction (1.00 = 100% 0.10 = 10%)
Machine setting, not a measurement

HCT

Hematocrit
Lab
%

HR

Heart Rate
Bedside EKG if no dZdt or Z0 present, otherwise IQ machine
Beats / Minute
10 – 15 cardiac contractions averaged

HR_mean

Heart Rate
HRV machine
beats/min
15 minutes integration time

L_mean

LFA (Low Frequency Area)
HR spectrum 0.04 – 0.10 Hz
HRV machine
Hz
15 minutes integration time

LR_mean

Ratio of L/R
Unitless
15 minutes integration time

MAP

Mean Arterial Pressure
Bedside monitor, most use A-line, some use cuff (only a very few).
Not indicated in data set which was used
mm Hg
10 – 20 seconds integration time

PAO2

Arterial Blood Gas O2 tension
Lab result
Torr

PAP

Pulmonary Arterial Pressure
PA Swan Ganz Catheter
mm Hg
~ 5 - 10 minutes integration time

PEEP

Positive End Expiratory Pressure
Respirator
mm Hg

Pox

(SapO2 from NICO, compared with SapO2 from Colin)
Pulse Oximetry
NICO
%
5 – 10 seconds integration time

PtcCO2

Transcutaneous CO2 Tension
Novametrics
Torr
30 seconds integration time

PtcO2

Transcutaneous Oxygen Tension
Novametrics
Torr
30 seconds integration time

Qs_Qt

Physiological Shunt Pulmonary Venous Admixture
amount of blood going through lungs w/o being oxygenated
Calculated from Swan-Ganz
%
15 minutes measurement time

R_mean

HFA (High Frequency Area)
HR spectral curve with a 0.10 Hz window around
fundamental respiratory frequency
HRV machine
Hz
15 minutes integration time

RR

Respiration Rate
Respirator
Breaths / Minute
30 – 60 seconds average

SAO2

Saturation of Arterial Hemoglobin
Lab result
%

SAPO2

Pulse Ox
Finger Cuff
%
5 – 10 seconds integration time

STAR

Goodness of ETCO2 measurement
NICO
1-5 stars

SVO2

Saturation Venous Oxygen
Lab Result
%

TCO2/F

Transcutaneous O2 / FIO2
Calculated from TCO2/FIO2
Torr
30 seconds integration time

TV

Tidal Volume
Respirator
liters
30 – 60 seconds integration time

VO2I

Oxygen Consumption Index
Calculated from Swan-Ganz TD cath, ICU computer
ml/minute/m^2
15 minutes measurement time

ZO

Baseline Bioimpedance
IQ machine
Ohms
12 - 15 beat integration

2.2.4 New Sensor Data

In year 2 of this program, EMR measurements made with the CapnoProbe sublingual CO_2 monitoring system will be processed and added to the database. The sublingual approach for measuring CO_2 was pioneered by Max Harry Weil (Institute of Critical Medicine, Palm Springs, CA). Subsequently, Optical Sensors Inc. (Minneapolis, MN) transformed the sublingual probe into an FDA-approved prototype (Model 2000) and then to a more economical handheld instrument (M80). This latter unit is marketed and sold by Nellcor Puritan Bennet, Inc. (Pleasanton, CA).

In a recent clinical study involving five normal human volunteers and 46 patients with acute life-threatening illnesses or injuries, sublingual P_{CO_2} proved to be a good estimator of severity of circulatory shock state [15]. It was found that when sublingual P_{CO_2} exceeded a well-defined threshold of 70 mm Hg, its positive predictive value for the presence of physical signs of circulatory shock was 1.00. When it was less than 70 mm Hg, it predicted survival with a predictive value of 0.93. A majority of patients in whom sublingual P_{CO_2} exceeded 70 mm Hg on admission, died in the hospital. It was concluded that noninvasive sublingual P_{CO_2} measurements may serve as a technically simple method for diagnosing and estimating the severity of circulatory shock states.

As part of the current project, comparisons will be made between transcutaneous measurements of CO_2 and sublingual measurements of CO_2. The potential use of sublingual CO_2 as an outcome predictor will be closely examined.

2.2.5 Improvements in Data Exchange at LAC+USCMC

During the current grant year, the automated patient monitoring system of the SICU was enhanced through the implementation of bi-directional communications with the hospital pharmacy and laboratory. This allows the complete history of patient medications, fluids, and laboratory results to be recalled as part of the SICU database. Thus, a computerized listing is now available beginning at the time of patient admission, and this information can readily be incorporated into the project database.

2.2.6 Database Organization

At the beginning of this project Geospace Research, Inc. (GRI) developed a custom PC computer architecture, and two identical PCs were designed and constructed. One was placed at GRI and the other was located at LAC+USCMC. These computers are used as database servers for workstations. Because the two computers are identical, the mobile database disks from one machine can be cloned and installed on the other. Thus, updating the two computer systems for the latest data additions is a simple process.

GRI evaluated two database programs (Oracle 9i and Sybase SQL Anywhere 8.0) before finally selecting the Sybase product for the current project. There are many reasons why Sybase is preferable. Sybase has a much better tool set and supports a publishable database; that is, it allows portions of the database to be transferred to a PDA, a laptop, or to a full server. Moreover, Sybase requires far fewer system resources than Oracle 9i. It is simple to administer and provides all of the functions necessary for the project. Sybase 8.0 is a workgroup version of the more comprehensive Sybase Enterprise program. The advantage of Sybase 8.0 is that the server operates peer-to-peer, and a server operating system is not required. If necessary, one could easily upgrade to Sybase Enterprise because the database formats are identical. However, this does not appear necessary on the basis of our first year results. In the current situation, Windows 2000 is used as the database

server operating system as well as the workstation operating system. This simplifies computer operations. Oracle 9i (like Sybase Enterprise) requires a server operating system. For our particular application, Oracle 9i is excessive and requires a steep learning curve. For comparison, Oracle 9i is distributed on 14 CD's, whereas Sybase 8.0 is contained on a single CD. Finally, we note that the SICU database discussed above is administered with Sybase Enterprise. As a result, the SICU data transfer is particularly easy. A schematic illustration of the medical database currently set up at GRI is shown in Figure 2 below.

As a matter of policy, *ad hoc* editing of data in the database is not permitted. All raw data table inputs are maintained in their original form. When necessary, new tables containing transformed and edited data are produced in addition to the original databases. These tables are created by executing SQL scripts. Desired data items are then consolidated into a single database using another set of SQL scripts. This policy allows our working database to be recreated at any time, with all editing and transformation steps clearly documented in the scripts. Only minor changes in the SQL scripts are necessary to run them under another database engine.

We found that running the mining and analysis tools on the same computer was problematic. (All computers discussed here have a Pentium IV, 2-GHz CPU with 1-GB memory; the operating system is Windows 2000 Professional.) The latest MATLAB software (version 13.0) now has a Java user interface. The MATLAB Database Toolbox interfaces with Sybase via Microsoft's ODBC drivers. Running Sybase, Java, MATLAB, and the ODBC on the same machine led to unacceptable processing delays. We obtained much better results by hosting MATLAB on a second machine and connecting it to the database via 100 MBPS Ethernet.

At present, we have not implemented the MATLAB Web Server illustrated in Figure 2. Doing so in the future would allow GRI mining library routines to be accessed by web forms. Results would be served up to remote users either as plots or data files. Currently, all data mining is done at the local system console using either a sequence of MATLAB commands or MATLAB scripts (i.e., m-files).

2.2.7 Quality Control

In principle, the construction of a large database is a simple matter, but in practice it is not. The reason for this is that errors and inconsistencies in the incoming data must be isolated and corrected. As the database becomes very large, this becomes a significant problem. The two databases that are most susceptible to keying errors are the TR and WCS database. The SICU data is less problematic because the data acquisition is highly automated, a review is required for data sign off, and supervisory software is used to prevent erroneously keyed entries from being inserted into the database.

Because the WCS database is in the form of Microsoft Excel spreadsheets, a series of data set transformations must be performed to convert it to Sybase format. To facilitate this process and to trap errors, each cell of the WCS spreadsheet is initially examined with the aid of a Visual Basic program. The program identifies cells that are improperly formatted (i.e. as a text string instead of a numeric value) and examines all data to make sure that parameter values fall within reasonable limits. If a data value is suspect, the problem is addressed using the original data records of W. C. Shoemaker to resolve the issue. Formatting errors prevent the translation of the Excel spreadsheet into Sybase, and it is much easier to identify them in Excel rather than through terminating errors in the translation programs. Excel formatting errors are often subtle; a text string of "10" is indistinguishable from the numerical value of 10 when viewed in the spreadsheet.

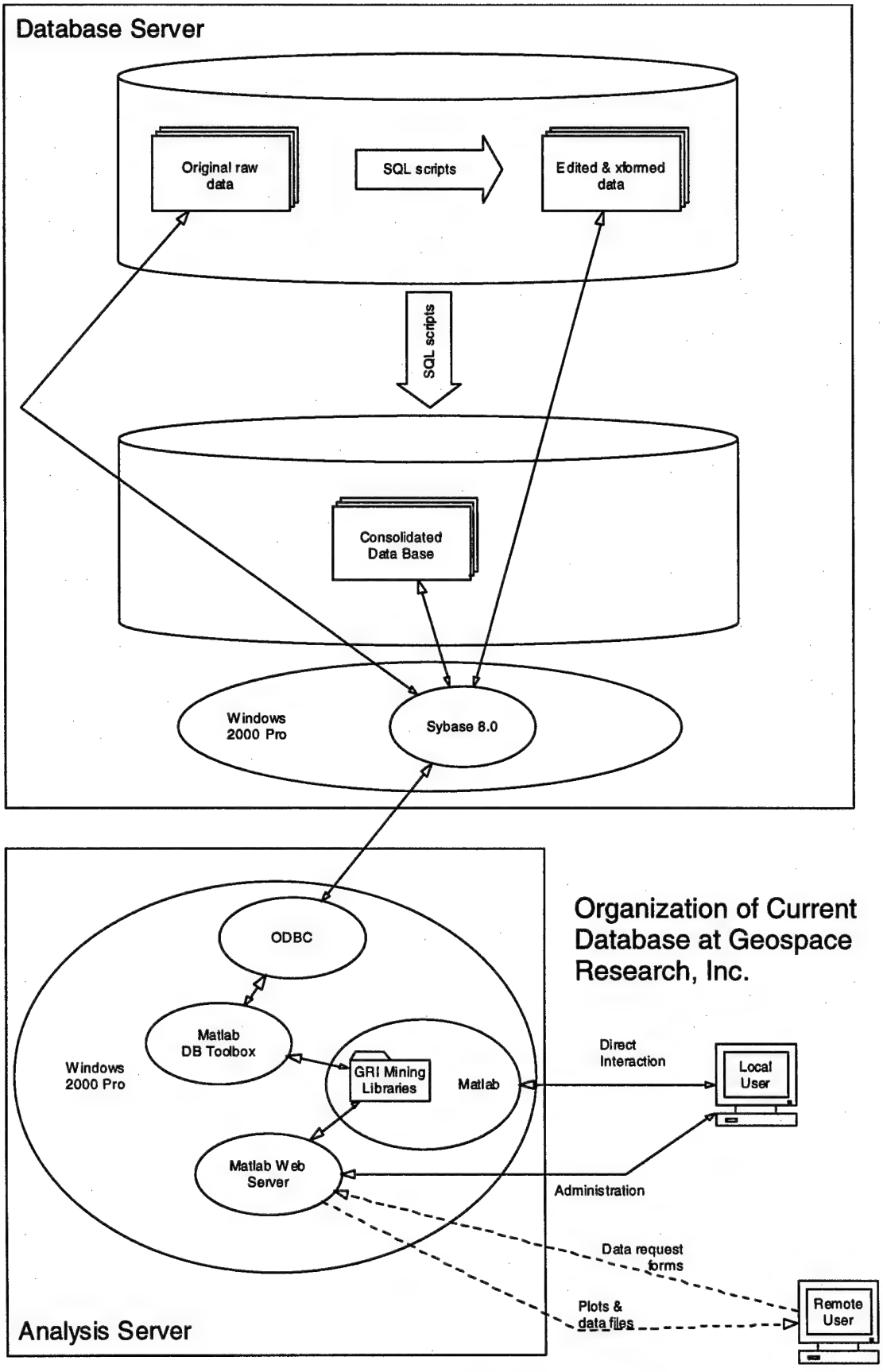

Figure 2. Database setup for the LAC+USCMC Medical Trauma Project.

The TR and the SICU databases are supplied as relational databases, so formatting is not an issue. However, the TR database structure does change with time. Both the TR database and the corrected WCS database are imported into the database program in the form of tables. Data in these "source tables" are never changed or edited. Instead, SQL macros are used in conjunction with the tables to create intermediate data tables. When new TR and/or WCS and/or SICU data is added to the system, new data sets are generated, and analyses are performed to determine whether parameter values are reasonable and whether overlapping data are consistent. For example, parameter distribution functions are examined, survivor/non-survivor values are cross referenced, and hard filtering limits are placed on some parameter values (e.g., blood alcohol level). It is also worth noting that a patient may show up as a survivor in the WCS database, and a non-survivor in the TR. In this case, the patient may have been followed for two weeks for the WCS database and determined to be survivor. However, on occasion patients subsequently undergo sudden downturns and do not survive. When an inconsistency is identified, an investigation must be launched to resolve the problem. This may involve locating a patient's archived medical chart, which can involve a search lasting several days.

Intermediate databases are necessary to correct errors identified in the original databases and to normalize certain parameter values. For example, because of a Y2K problem in the TR, one patient's age showed up as 137. The Y2K algorithm error was identified and corrected as part of the macro that created an intermediate database. The original data remains unchanged, and the macro serves as documentation of the changes made. The macros can be quite long because they contain information about specific data values that have been corrected, data transformations that have been performed, and data normalization procedures that have been implemented. In the latter case, values for cardiac output, DO_2, VO_2 etc. may have to be indexed prior to inclusion in the main database. Once again these corrections show up in lines of SQL code in a macro.

When all corrections are made and verified, the new data is finally incorporated in the Main Project Database. Although the words "seamlessly add new patient data to the database" were used in the original statement of work, it is clear that the necessary quality control measures prevent this activity from being truly seamless during the entry process. However, the final Project Database itself is seamless.

2.2.8 Outcome Prediction With the Main Project Database

Many different data items and relationships can be extracted from the current database. Figure 3 shows a plot of the average Cardiac Index (CI), Heart Rate (HR), Mean Arterial Pressure (MAP), percentage oxyhemoglobin saturation ($SapO_2$), and transcutaneous O_2 tension divided by fractional inspired oxygen concentration ($PtcO_2/FIO_2$) versus time after admission to the LAC+USCMC emergency department. Patients with head trauma are not included in the sample population because of the unique type of hemodynamic pattern associated with head injury. Standard deviations are estimated from the data used to calculate mean values; they represent the spread in the distribution of data values about the mean. Results are shown in Figure 3 for survivors (blue) and non-survivors (red). A good predictor yields a large separation between the parameter distribution functions of survivors and non-survivors. It is clear that $PtcO_2/FIO_2$ in itself is a fairly good predictor of outcome, particularly at the earliest times after the trauma victim enters the hospital. The large $PtcO_2/FIO_2$ standard deviation for non-survivors near 10 hours is caused by a low patient count at this time. Other parameters shown in Figure 3 are not good predictors because they fail to produce large separations in survivor/non-survivor distribution functions. As noted in Section 2.1.2 many outcome predictors are currently being assessed as part of a more generalized

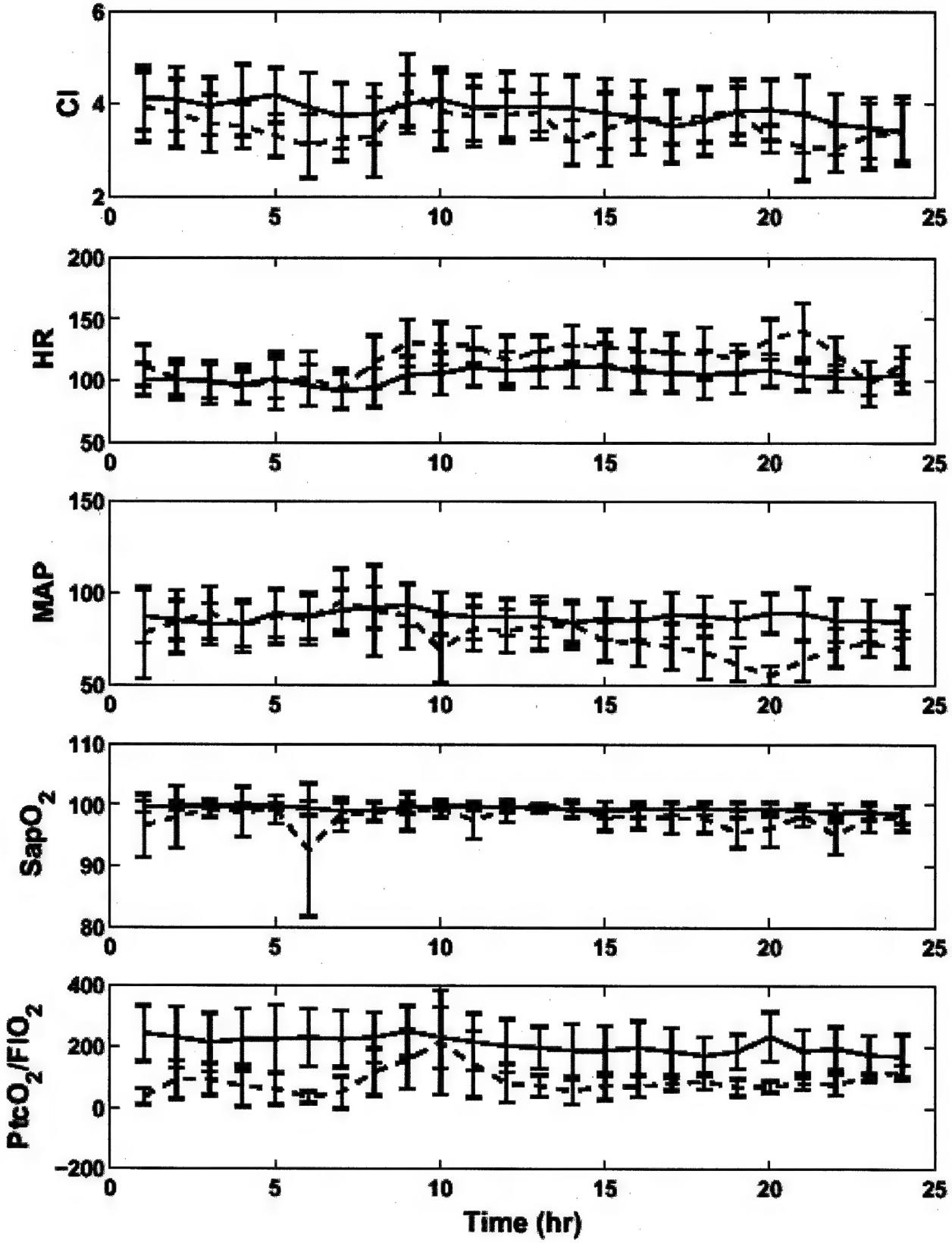

Figure 3. Mean values and standard deviations of five hemodynamic parameters in the Database. Blue designates survivors, whereas red represents non-survivors. PtcO2/FIO2 exhibits the greatest population separation and is therefore the best outcome predictor.

study. These include initial heart rate, initial MAP, lowest MAP, initial cardiac index, APACHE II score, predictions of discriminant analysis, probability analysis based on the "nearest neighbors" of a patient's "state vector," $PtcO_2/FIO_2$, and the combination of $PtcO_2/FIO_2$ and $PtcCO_2$. At present the mathematical "nearest neighbor" analysis appears to be the best technique for outcome prediction, whereas $PtcO_2/FIO_2$ has emerged as the best single parameter predictor.

Our search for optimum predictors of survival/non-survival is centered on finding physiological parameters that yield the maximum possible separation in distribution functions of survivors and non-survivors. In this regard, one examines positive (non-survival) and negative (survival) predictability. To measure the effectiveness of the predictor, one uses indices such as sensitivity (number who are positive and test positive/number who are positive) and specificity (number who are both negative and test negative/number who are negative). Initially the quantity S = [(1-sensitivity)^2 + (1- specificity)^2] is minimized to establish a nominal parameter threshold and two-sided tests are used to determine the most promising predictors. Subsequently, trade-offs between sensitivity and specificity are made to arrive at the optimum parameter threshold. This methodology is not unlike that employed to interpret laboratory tests or to diagnose disease with clinical data. In our case, sensitivity measures how well the physiological quantity identifies those who do not survive, that is, how sensitive it is. If a test has a high sensitivity, it will pick up nearly everyone who does not survive. Specificity measures how well the test excludes those who survive, that is, how specific it is. If a test has a very high specificity, it won't misclassify many survivors as non-survivors. Typically, one analyzes curves of sensitivity versus (1-specificity) to establish an optimum cutoff value.

The disadvantage of the sensitivity and specificity parameters is that they do not assess the accuracy of the test in a clinically useful way. However, they do have the advantage that they are not affected by the proportion of the trauma victims that do not survive, which is called prevalence. The effect of lower prevalence is much as one would expect: the lower the number of non-survivors in the study, the more certain we can be that a negative test indicates survival of a trauma patient, and the less sure that a positive result really indicates that the trauma victim did not survive. In the current investigation, predictive uncertainty is reflected in the t value of the double-ended Student's t distribution and in the fitting errors of sensitivity and specificity obtained when the quantity S is minimized. Because the prevalence of non-survivors is high in our study (20-25%), the uncertainty of the predictions is relatively low.

Software has been written to automatically examine the predictive values of a large number of parameters. The predictor analysis involves least-squares fitting to minimize S and yields sensitivity and error in sensitivity, specificity and error in specificity, optimum parameter threshold, mean of parameter value in non-survivors, mean of parameter value in survivors, standard deviations for the non-survivor and survivor distribution functions, and the t value for the double ended Student's t Distribution. The main W. C. Shoemaker database consisting of 689 patients is used as a derivation data set to search for predictors. A separate validation data set is being developed to confirm the predictors. The derivation data set is always subject to bias because the same data used to derive a predictor is also used to test its effectiveness. Consequently, there is a large program emphasis on securing more patient case histories. This is evidenced by the 40% increase in total number of EMR trauma patients processed during the current grant year.

3 Key Research Accomplishments

1. The stage 1 development of a large national trauma database for studying hemodyanamics including blood flow and tissue perfusion failure was completed.
   - The database is unbiased, high in quality, well and clearly defined, and can be independently mined by members of the combat-casualty-care community.
   - Mining of the database provides insight into the resuscitative outcome of combat casualties and civilian trauma victims.
   - The database can be used to help determine when to resuscitate, how to resuscitate, and what the end point of resuscitation should be.

2. An evaluation of outcome predictors indicates that a mathematical "nearest neighbor" analysis is the best technique identified and applied to the database for predicting survival/non-survival, whereas $PtcO_2/FIO_2$ has emerged as the best single parameter predictor.
   - Outcome predictors greatly facilitate the triage process for combat casualties and measure the effectiveness of the resuscitation effort.
   - Outcome predictors together with the analyses of hemodynamic patterns allow hospitals to identify patients who are at risk in the earliest stage of the therapeutic process, adjust therapies to improve outcomes, and promptly determine whether the new therapy will lead to survival.

4 Reportable Outcomes

4.1 Publications

1. Shoemaker WC, Wo CCJ, Botnan A, Bayard DS, Jelliffe RW: Development of a hemodynamic database in severe trauma patients to define optimal goals and predict outcome. IEEE Transactions on Automatic Control 2001; 36: No. 9, 231-236
2. Bayard DS, Botnan A, Shoemaker WC, Jelliffe RW: Stochastic analysis of therapeutic modalities using a database of patient responses. IEEE Transactions on Automatic Control 2001; 36:No. 9, 439-444
3. Shoemaker, WC, Wo CCJ, Chan L, Ramicone E, et al: Outcome prediction of emergency patients by noninvasive hemodynamic monitoring. Chest 2001; 120:528-537
4. Olinski M, Shoemaker WC, Reis E, Kerstein M: Current controversies in shock and resuscitation. Surg Clin North America 2001; 81:1217-1252
5. Shoemaker WC: New approaches to trauma management using severity of illness and outcome prediction based on noninvasive hemodynamic monitoring. Surg Clin N Am 2002; 82:245-255
6. Kern J, Shoemaker WC: Meta-analysis of hemodynamic optimization in high risk patients. Crit Care Med 2002; 30:1686-1692
7. Shoemaker WC, Bayard DS, Wo CCJ, Botnan A, Chan L, Jelliffe RW, Djuth FT, Belzberg H: Noninvasive hemodynamic monitoring of emergency patients for outcome prediction by a stochastic control program. Crit Care Med 2002, Submitted
8. Fathizedeh P, Shoemaker WC, Wo CCJ, Colombo J: Autonomic activity in trauma patients based on variability of heart rate and respiratory rate. Crit Care Med 2002, Submitted

4.2 Presentations

1. Shoemaker WC: Noninvasive monitoring of high risk patients using a new stochastic analysis and control system. Aukland, New Zealand April 8, 2002.
2. Shoemaker WC: Noninvasive monitoring of high risk patients using a new stochastic analysis and control system. Christchurch, New Zealand. April 10, 2002.
3. Shoemaker WC: Noninvasive monitoring of high risk patients using a new stochastic analysis and control system. Wellington, New Zealand, April 12, 2002.
4. Shoemaker WC: Noninvasive monitoring of high risk trauma patients using a new outcome predictor, stochastic analysis and therapeutic decision support programs. Sacramento County Trauma Service, Roseland Hospital, Sacramento CA. May 30, 2002.
5. Shoemaker WC: Noninvasive monitoring of high risk patients using a new stochastic analysis and control system for outcome prediction and therapeutic decision support system. Frankfort, Germany, June 6, 2002.
6. Shoemaker WC: Outcome prediction and decision support program in high risk trauma and surgical patients using a new stochastic analysis with a control system and a therapeutic decision support program. Berlin University, Germany, June 10, 2002.
7. Shoemaker WC: Noninvasive hemodynamic monitoring of high risk patients using a new stochastic analysis for outcome prediction therapeutic decisions. Mexican Pediatric Society, International Conference, Mexico City, Mexico, June 20, 2002.
8. Djuth FT, Belzberg H, Shoemaker WC, Elder JH, Zhu J, Wo CCJ: An open trauma database for studying hemodynamics including blood Flow and tissue perfusion failure, ATACCC Meeting, St. Pete Beach, FL, September 9-13, 2002.
9. Belzberg H, Elder JH, Djuth FT, Oder D, Shoemaker WC: The developing of a Trauma Outcome Data Analysis (TODA) tool: answering old questions with new techniques: ATACCC Meeting, St. Pete Beach, FL, September 9-13, 2002.
10. Shoemaker WC, Belzberg H, Bayard DS, Wo CCJ, Botnen A, Djuth FT, Choi A, Jelliffe, RW: Noninvasive hemodynamic monitoring of trauma patients for outcome prediction and decision support by a stochastic control analysis and display, ATACCC Meeting, St. Pete Beach, FL, September 9-13, 2002.
11. Shoemaker W.C: Outcome prediction in high-risk patients using noninvasive monitoring and a new stochastic analysis. USC Pharmacology workshop, Sept 30 –Oct 2, 2002.

4.3 Databases

1. EMR test (Toy) database consisting of 53 trauma patients common to the WCS database (Heart Rate Variability data set), the Surgical Intensive Care Unit database, and the Trauma Registry database.

2. EMR Main Project Database consisting of 689 trauma patients from the WCS data sets and corresponding patient data from the Trauma Registry. The patients were monitored with state-of-the-art non-invasive sensors as well as with invasive techniques and procedures. This database is considered to be very high in quality because the diagnostic measurements are comprehensive, and the prevalence of non-survivors is high.

5 Conclusions

The evolving trauma database developed as part of this project serves as a tool for understanding the resuscitation process. The further development of appropriate methodologies and tools for mining the database will greatly improve the quality of trauma care for both the combat casualty and the civilian trauma victim. The organized database supports analyses, evaluations, and data mining by diagnostic and covariate categories, as well as by temporal patterns of hemodynamic patterns in survivors and nonsurvivors. Our preliminary results indicate that the new outcome predictor(s) are greater than 90% correct within the first 12 to 24 hours after emergency department admission. On the basis of such measurements, a therapeutic decision support and predictive modeling system is being developed that relies primarily on the hemodynamic patterns of survivors and their response to therapy.

5.1 Suggested Changes

During the first year of work, it became clear that more existing medical record (EMR) patient data will greatly enhance the trauma database and support complex methodologies used to mine the database. In response to this need, additional EMR data were processed during the first grant year. The concept of prospective data acquisition suggested in the Year 2 statement of work will not generate the large number of trauma cases necessary to meet the emerging needs of the program. However, the processing of an ever increasing supply of EMR patient data will. Therefore, we suggest that paragraph two of the Year 2 statement of work be replaced by the following:

"During the second grant year, additional, newly acquired, existing medical record patient data will be processed, analyzed, interpreted, and incorporated into the Main Project Database without the possibility of patient identification."

A related e-mail communication from Dr. Maryann F. Pranulis, AMEX/AMEDD, is included as an attachment to this annual report.

5.2 Importance

The development of the current trauma database is expected to greatly improve the quality of trauma care for both the combat casualty and the civilian trauma victim. Taken as a whole, this new database and associated mining tools allow optimum resuscitation approaches to be developed and provide a means for measuring, validating and implementing new physiological sensor strategies. At present, it also appears that a new therapeutic decision support system for trauma physicians will be an important spin-off of this project. The Main Project Database is open to other investigators, contains an ever increasing number of high-quality well-documented trauma cases, and accommodates new state-of-the-art, FDA-approved sensors and techniques. As a result, the time line required to develop more effective therapies and translate this research into clinical practice will be much shorter than in previous studies of this nature.

6 References

1. Shoemaker WC, Wo CCJ, Botnan A, Bayard DS, Jelliffe RW: Development of a hemodynamic database in severe trauma patients to define optimal goals and predict outcome. IEEE Transactions on Automatic Control 2001; 36: No. 9, 231-236

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3. Shoemaker WC, Bayard DS, Wo CCJ, Botnan A, Chan L, Jelliffe RW, Djuth FT, Belzberg H: Noninvasive hemodynamic monitoring of emergency patients for outcome prediction by a stochastic control program. Crit Care Med 2002, Submitted

4. Shoemaker WC: New approaches to trauma management using severity of illness and outcome prediction based on noninvasive hemodynamic monitoring. Surg Clin N Am 2002; 82:245-255

5. Dunham CM, Cowley RA, Gens DR, Ramzy AJ, Rodriguez A, Belzberg H, Wiles CE: Methodologic approach for a large functional trauma registry. MMJ 1989; 38:227-233

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7. Shoemaker, WC, Wo CCJ, Chan L, Ramicone E, et al: Outcome prediction of emergency patients by noninvasive hemodynamic monitoring. Chest 2001; 120:528-537

8. Fathizedeh P, Shoemaker WC, Wo CCJ, Colombo J: Autonomic activity in trauma patients based on variability of heart rate and respiratory rate. Crit Care Med 2002, Submitted

9. Olinski M, Shoemaker WC, Reis E, Kerstein M: Current controversies in shock and resuscitation. Surg Clin North America 2001; 81:1217-1252

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11. Shoemaker WC, Bayard DS, Wo CCJ, Botnan A, Chan L, Jelliffe RW, Djuth FT, Belzberg H: Noninvasive hemodynamic monitoring of emergency patients for outcome prediction by a stochastic control program. Crit Care Med 2002, Submitted

12. Shoemaker WC, Thangathurai D, Wo CCJ, Kuchta K, Canas, M, Sullivan MJ, Farlo J, Roffey P, Zellman V, Katz RL: Intraoperative evaluation of tissue perfusion in high-risk patients by invasive and noninvasive hemodynamic monitoring. Crit Care Med 1999; 27:2147-2299

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15. Weil MH, Nakagawa Y, Tang W, Sato Y, Ercoli F, Finegan R, Grayman G, Bisera J: Sublingual capnometry: A new noninvasive measurement for diagnosis and quantitation of severity of circulatory shock. Crit Care Med 1999; 27:1225-1229

7 Appendices

1. Recent e-mail communication from Dr. Maryann F. Pranulis, human subjects protection scientist, AMEX/AMEDD, concerning the approval of exempt status and the elimination of a prospective study.

2. Copies of eight publications listed in Section 4 above.

Date: Wed, 02 Oct 2002 15:53:09 -0400
From: "Pranulis, Maryann F Dr AMDEX" <Maryann.Pranulis@DET.AMEDD.ARMY.MIL>
Subject: RE: A-10847, DAMD17-01-2-0823, proposal 00089002,
Studies of Tissue Perfusion Failure at LAC & USCM...
To: 'Howard Belzberg' <belzberg@usc.edu>
Cc: "Stotler, Karen S Ms USAMRAA" <Karen.Stotler@DET.AMEDD.ARMY.MIL>,
"Vandre, Robert H COL USAMRMC" <Robert.Vandre@DET.AMEDD.ARMY.MIL>,
"Zadinsky, Julie K COL USAMRMC" <Julie.Zadinsky@DET.AMEDD.ARMY.MIL>,
"Pranulis, Maryann F Dr AMDEX" <Maryann.Pranulis@DET.AMEDD.ARMY.MIL>
X-Mailer: Internet Mail Service (5.5.2656.59)
Importance: high

Dr. Belzberg:

It was a pleasure to talk with you today and to learn that the retrospective component of this award has yielded sufficient data to delay or outright drop doing a prospective study.

As I understand from our discussion, you have made no changes to the retrospective component that was approved as exempt on 29 September 2001. So long as there are no changes in venue, investigators, procedures, or data base that will be used, and you are still using de-identified, existing medical record data, the previous approval of exempt status is still valid. However, it should be noted that the cited approval restricted you from recruiting and/or enrolling any human subjects or using any prospectively collected human subjects data. The approval was also only for use of the trauma data base at the Los Angeles County and University of Southern California Medical Center Surgical Intensive Care Unit. These restrictions are still in effect.

If there are any modifications in the previously approved-as-exempt protocol, then you are required to either submit, for HSRRB review and approval, a new protocol or a request for an amendment to the approved version prior to implementing the change. If the USC- IRB changes the designation from exempt to non-exempt, please notify this office and you will be advised of the procedures that need to be followed.

Best wishes for continued success in this important endeavor. If you have any questions or concerns about the human subjects aspects of this project, please let me know.

Maryann F. Pranulis, RN, DNSc
Human Subjects Protection Scientist
AMDEX
maryann.pranulis@det.amedd.army.mil
(301) 619-6240
FAX (301) 619-7803

Message-ID: <5.0.2.1.1.20021002104711.00ab7140@email.usc.edu>
From: Howard Belzberg <belzberg@usc.edu>
To: maryann.pranulis@det.amedd.army.mil
Subject:
Date: Wed, 2 Oct 2002 14:06:58 -0400
MIME-Version: 1.0
X-Mailer: Internet Mail Service (5.5.2656.59)

Content-Type: multipart/alternative;
boundary="----_=_NextPart_003_01C26A4D.5513C420"

Dear Dr. Pranulis,
In regard to our project (contract no. DAMD 17-01-2-0070) we plan to modify our plans for year 2. After review of our first year's acquisition of patients using retrospective de-identified data, and discussions with our sponsor, we do not plan to persue the prospective component of the project at the present time. These changes will be outlined in our annual report to be submitted by October 28, 2002. In light of these changes we would request that the previously granted exemption be continued.

Thank you,
Howard Belzberg, M.D.

Development of a Hemodynamic Database in Severe Trauma Patients to Define Optimal Goals and Predict Outcome.

WC Shoemaker [1], CCJ Wo[1], A Botnen[2], DS Bayard[3], RW Jelliffe[2]

Department of Surgery and Anesthesia [1], Laboratory of Applied Pharmacokinetics [2], University of Southern California, School of Medicine, Los Angeles CA 90033 and Jet Propulsion Laboratory [3], Pasadena CA 91109

Abstract

Noninvasive hemodynamic monitoring systems provide continuously monitored on-line displays of data from emergency department admission to the OR, and to the ICU for early recognition of circulatory dysfunction in acute emergency conditions. The net cumulative deficits of cardiac index are estimated by thoracic electric bioimpedance, arterial hypoxemia is measured by pulse oximetry, and tissue perfusion is reflected by transcutaneous pO_2. Based on a large database, survival was satisfactorily predicted by discriminant analysis and by a new stochastic analysis and control program.

1. Introduction

We studied sequential hemodynamic patterns of surviving and nonsurviving postoperative patients, and used the temporal circulatory patterns of survivors in the first 12 hours postoperatively after severe trauma as a first approximation to define optimal goals of therapy and the patterns of nonsurvivors as early warning signs of potential disasters [1,2].

Goal-directed therapy has been used as a strategy for high-risk surgery and acute illness such as trauma [1-7]. Although most shock studies have demonstrated that early diagnosis and vigorous therapeutic interventions were keys to success, early diagnosis of circulatory dysfunction is difficult, because traditionally shock has been recognized by imprecise signs and observer-dependant subjective symptoms. Shock is easy to recognize in its later stages by hypotension, oliguria, and collapse, but by that time, therapy is often ineffective.

Noninvasive hemodynamic monitoring technology has now become available throughout the hospital including the emergency department (ED), operating room (OR), post-anesthesia recovery room, ICU, step down units, hospital floors, prehospital areas, and doctors' offices. Noninvasive monitoring is easier, faster, safer, cheaper and equally sensitive. [8-14].

The major lesson learned from earlier studies is that effective resuscitation of acute life-threatening emergencies requires achieving optimal physiological goals as early as possible: if

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circulatory mechanisms can be identified earlier and treated more vigorously to specified physiologic criteria, outcomes should be improved.

We have developed a large database of invasive and noninvasive hemodynamic monitoring of acutely ill trauma and surgical emergencies beginning in the emergency department (ED): a) to describe early survivor and nonsurvivor patterns of emergency patients in terms of cardiac, pulmonary, and tissue perfusion deficiencies; b) to measure quantitatively the net cumulative amount of deficit or excess of the monitored functions that correlate with survival or death; and c) to use discriminant analysis to predict outcome and evaluate the biological significance of monitored deficits (13).

2. Methods

2.1 Development of databases

Databases for acute injury patients (N=316), elective high risk surgery, noninvasively monitored patients (N=374) and invasively monitored patients (N=809), septic shock patients (N=378), and hemorrhage only patients (N= 87) have been developed to describe the primary injuries or illnesses, the hemodynamic patterns by invasive and noninvasive methods, and their outcomes, including survival/nonsurvival, organ failure, other complications, time of ED admission, hospital days, ICU days and estimated hospital costs. Noninvasive monitoring was begun in the ED and followed to the OR, radiology department and ICU; invasive pulmonary artery catheterization (PAC) was instituted when clinically indicated after arrival in the ICU.

We have developed a large database with over 10,000 time lines describing the clinical and hemodynamic patterns of 30 clinical subsets with specified co-morbid conditions, 18 hemodynamic variables, and over 2500 therapeutic interventions with values obtained before, during, and after each therapy given one-at-a-time, except for clinical exigencies.

The sequential patterns were described in time elapsed from onset of illness or in time from ED admission. Weighting criteria to specify the nearest neighbors were based upon the clinical diagnosis, co-morbid conditions, and hemodynamic patterns of survivors vs. nonsurvivors. The p values of differences in the temporal patterns of survivors' and nonsurvivors' values were used as weighting criteria in each subset, for example, for subsets of patients with and without head injuries, blunt vs. penetrating trauma, truncal and nontruncal trauma, age stratifications, prior cardiac, respiratory, hepatic, and renal dysfunction or organ failure, etc.

Finally, the hemodynamic responses to standardized test doses of whole blood or packed red cell transfusions given over a specified period of time (usually 1-hour) provide quantitative measures of each patient's cardiac reserve capacity. This is expressed as changes in cardiac index relative to corresponding change in PA occlusion (wedge) pressure or central venous pressure (Starling's myocardial performance curve) before and after a blood transfusion given over a one-hour period. Criteria for satisfactory vs. limited cardiac functional reserve capacity have been developed for each clinical subset and each time period.

2.2 Noninvasive Hemodynamic Monitoring Systems

The monitoring systems are an improved noninvasive thoracic electric bioimpedance cardiac output device, a pulse oximeter to measure arterial hemoglobin saturation, a noninvasive blood pressure device, and transcutaneous O_2 and CO_2 sensors to reflect tissue perfusion/oxygenation. These continuously monitored noninvasive measurements were used to prospectively evaluate circulatory patterns in 151 consecutively monitored severely injured patients beginning with admission to the emergency department in a university run county

hospital. The net cumulative deficit or excess of each monitored parameter was calculated as the cumulative difference from the normal value versus the time-integrated monitored curve for each patient. The deficits of cardiac, pulmonary, and tissue perfusion functions were analyzed in relation to outcome by discriminant analysis and crossvalidated.

Noninvasive monitoring compared favorably with invasive thermodilution catheter monitoring in high risk patients with surgery, blunt trauma, gunshot wounds, head injuries, sepsis, strokes, drug overdose, myocardial infarction, and acute gastrointestinal bleeding. Differences between impedance and thermodilution cardiac output estimations were more than offset by the continuous on-line display of data that allowed instant recognition of changes in the course of a patient's illness, calculation of the deficit of each monitored variable, and evaluation of therapeutic responses.

3. Results

3.1 Therapeutic Goals

The specific monitored goals of therapy based on empirical findings of survivors were: cardiac index > 4.5 L/min/m^2; systolic blood pressure > 120 mmHg; pulse oximetry > 96%; transcutaneous oxygen $PtcO_2/FiO_2$ ratio >200; heart rate < 100 beats/min (1,3).

3.2 Survivor and Nonsurvivor Hemodynamic Patterns in High-risk Surgery, Trauma, and Sepsis

In nonsurvivors, the initial hemodynamic changes consisted of reduced cardiac index, oxygen delivery, and oxygen consumption. Shortly after surgery, the survivors had hemodynamic and oxygen transport values greater than normal, and greater than those in the nonsurvivors. Similarly, in severely traumatized patients and in both medical and surgical septic shock patients, survivors also had increased hemodynamic and oxygen transport values, suggesting that these responses were compensating for prior inadequacies of tissue perfusion and oxygenation.

3.3 Quantitative Assessment of Continuously Monitored Noninvasive Variables as Net Cumulative Amount of Excess or Deficit

Many recordings show considerable variability which may obscure the underlying pattern. To overcome this problem we evaluated the net cumulative deficit or excess in cardiac, pulmonary, and tissue perfusion function data by integrating over time the area between the monitored curve and the normal or optimal values. In nonsurviving patients, the mean values as well as the net cumulative deficits were significantly greater for cardiac index, tissue perfusion, and arterial saturation than in survivors, even though the survivors' and nonsurvivors' MAP values were not significantly different.

3.4 Outcome Prediction by Discriminant Analysis

The data were analyzed by discriminant function (15). The following variables were selected by the stepwise discriminant analysis (PROC STEPDISC): a) cumulative $PtcO_2/FiO_2$, b) Glasgow coma score, c) cumulative $SapO_2$ values and d) cumulative cardiac index. Based on the classification function generated for each of these four variables in PROC DISCRIM, discriminant function, Z, was derived for an individual patient: Z = 0.0011a + 0.3300

+ 0.0656c + 0.0423d; where "a" represents cumulative $PtcO_2/FiO_2$ value, "b" represents Glasgow coma score, "c" represents cumulative $SapO_2$ value and "d" represents cumulative cardiac index value. Classification of the survivors was: Z>2.36. Half of the cases were randomly selected to serve as the calibration data set; the other half was used as the validation data set. As shown in Figure 1, above, there were 14/76 (18.4%) misclassifications in the cross-validation study, compared with 23/151 (15.2%) of the series as a whole. This was considered to be in reasonably satisfactory agreement (14). Using stepwise discriminant analysis; 95 % of the survivors and 62% of the nonsurvivors were correctly classified in the early period after the initial resuscitation.

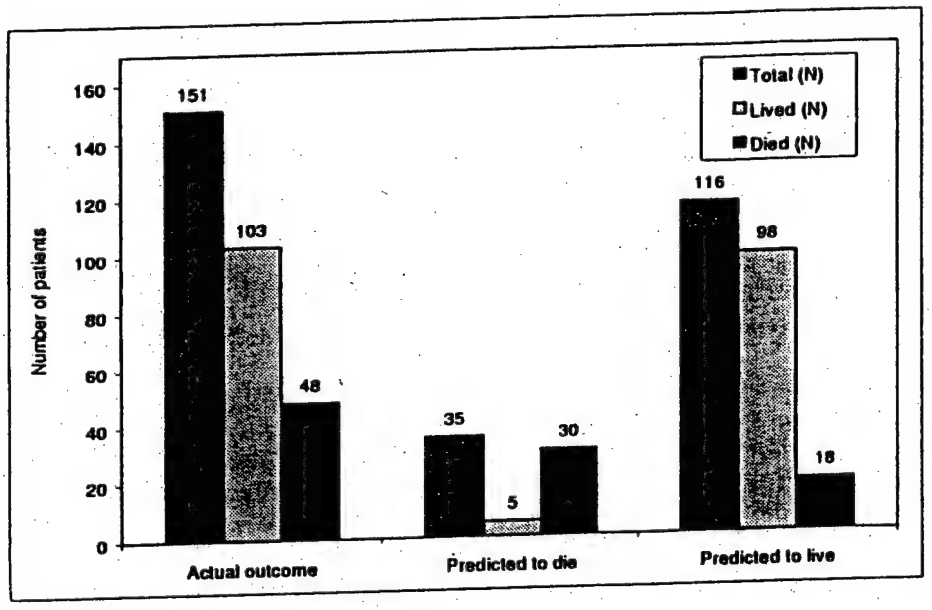

Figure 1. Classification Summary for the Series (N=151)

4. Conclusion

Hemodynamic data obtained by pulmonary artery (PA) thermodilution (Swan-Ganz) catheter have shown significantly higher hemodynamic and oxygen transport values in survivors compared with nonsurvivors (1,2,4-12). Classically, shock is often diagnosed by oliguria, hypotension, and collapse in the late stage, when therapy is least effective. However, initially we recognized shock by subjectively evaluated signs and symptoms such as skin color, skin temperature, mental status, weak thready pulse, and vital signs. The conventional therapeutic approach has been to correct these superficial manifestations as soon as they are recognized, but underlying hemodynamic mechanisms are often not corrected (13,14).

The data suggest that multiple noninvasive monitoring systems are feasible methods to supply information previously available only in the catheterization lab under sterile operating room (OR) conditions or by the PA (Swan-Ganz) catheter under critical care conditions. The data are sufficiently close to the information supplied by the PA catheter to be a useful surrogate for invasive monitoring. Moreover, they can be used throughout the hospital in the

early period immediately after emergency department admission. They provide continuous on-line displays rather than "snapshots" at infrequent intervals.

Most importantly, in the period during and immediately after resuscitation, noninvasive hemodynamic patterns of patients with severe trauma are closely related to outcome. We have used these patterns to develop outcome predictors by discriminate analysis to elucidate underlying mechanisms (13). Also we now propose to supplement or replace discriminate analysis with a stochastic control program, which is a more powerful research tool applicable to more extensive use of monitored variables in a wider variety of acutely ill patients.

The data show that the initial hemodynamic findings are low flow or unevenly distributed microcirculatory flow with poor tissue perfusion/oxygenation; these are initially precipitated by many factors including hypoxemia, hypovolemia, acidosis, and the adrenomedullary stress response. The poorly perfused, acidotic capillary endothelial wall activates macrophages, stimulates the systemic immune response syndrome (SIRS), and produces reactive oxygen substances (ROS), that may contribute to the development of ARDS and other organ failures.

Our hypothesis is that early identification of the initiating hemodynamic mechanisms allows their correction with concomitant reversal of shock and improved outcome. Preliminary data demonstrated that the stochastic control program provides objective, quantitative information on the likelihood of survival or death before and after each therapy. In essence, the stochastic control program provides early warning of initiating mechanisms at times when they can be reversed, evaluates the relative efficacy of specific therapy to reverse early deleterious mechanisms, and thereby provides the basis for understanding of the contributory role of these hemodynamic mechanisms.

This analysis is based on the assumption that it may be easier and more efficacious to identify initiating hemodynamic mechanisms of shock and lethal organ failure by evaluation of early hemodynamic patterns and their transitions after therapeutic interventions. Transitional states after therapeutic interventions also may be evaluated in terms of possible mechanisms; for example, cardiac reserve capacity may be inferred from changes in myocardial performance after a standardized transfusion of 1 unit of whole blood given over a 1-hour period or a standardized test dose of dobutamine. A distinction is made between initiating hemodynamic mechanisms and later immunochemical or other biochemical mediators of organ failure.

Outcome predictors will be used to fine tune evolving hemodynamic patterns and to observe the effects of modifying potentially lethal mechanisms by therapy early in the course of acute illness. The assumption is that there are different types and degrees of hemodynamic dysfunction that need objective measures to track their presence and intensity. An objective outcome measure representing the probability of survival should be a useful means to evaluate the evolution of acute illnesses that lead to organ failures. Trauma and high-risk surgical patients were selected because of their varying hemodynamic patterns, severity of illness, and associated co-morbid conditions.

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Stochastic Analysis of Therapeutic Modalities Using a Database of Patient Responses

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Abstract

This paper proposes a new method for stochastic analysis and control which does not require a model, but which is constructed directly from a raw database of patient responses to therapy. Roughly speaking, the basic idea is to evaluate a control (a therapeutic policy or modality) which has, on the average, proved to work well for similar patients in the database. By "similar" is meant patients who have the same covariates and who are in similar dynamical states. These concepts will be made more precise in the paper. The proposed stochastic analysis and control approach for databases is new, although it is motivated by methods of machine learning put forth in [1][2] and methods of dynamic programming for stochastic control given in [3][4].

1. Concept of State

The first key step is to develop the definition of a "state" for a given patient in the database at a given stage of treatment. Many definitions of state are possible. Since we are working with a database of measurements, it is useful to define the state vector directly in terms of the available measurement information. Assume there are L different types of measurements obtained on a given patient (e.g., cardiac index, blood pressure, pulse oximetry, transcutaneous O_2 and CO_2 tensions, etc.). Then for each measurement type, denoted as y_l, define the state vector as a concatenation of the value y_l itself, with its first and second time derivatives $\dot{y}_l$, $\ddot{y}_l$, and with its first integral $\int y_l dt$, as follows,

$$x(t_k) = \left[y_1(t_k), \dot{y}_1(t_k), \ddot{y}_1(t_k), \int_0^{t_k} y_1 dt, \ldots\ldots, y_L(t_k), \dot{y}_L(t_k), \ddot{y}_L(t_k), \int_0^{t_k} y_L dt \right] \quad (1)$$

2. Implicit Dynamic model

It is convenient to think of the propagation of the patient's state x_k at time t_k, to his state x_{k+1} at time t_{k+1} as obeying the following nonlinear dynamical system with process noise w_k, parameter vector p, and control u_i i.e.,

$$x_{k+1} = f(x_k, u_i, p, w_k) \quad (2)$$

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For simplicity, p is assumed to be drawn from a finite set formed by enumerating all useful combinations of covariates,

$$p \in \{p_1, \ldots, p_M\} \tag{3}$$

Both the parameter vector p of covariates and process noise w help to explain the variability of responses seen in the database. Specifically, the covariates help to distinguish gross differences in responses due to major categories of complications (e.g., with vs. without head injuries, blunt vs. penetrating trauma, truncal vs. nontruncal trauma, age stratifications, etc.) On the other hand, process noise helps to explain smaller differences between patients with identical covariates but with different responses to the same therapy.

3. Control Inputs

It will be assumed that there is only a finite set of M control inputs in (2) that can be applied to the system. Specifically, the control $u(t_k)$ at time t_k is assumed to be drawn from the finite set,

$$u(t_k) \in \{u_1, \ldots, u_M\} \tag{4}$$

where u_i are controls (therapeutic modalities) such as fluid therapy with crystalloids, with colloids, with whole blood or packed RBC's, or various vasoactive drugs such as dobutamine, dopamine, and other possible modalities.

4. Nearest Neighbors

Once the state vector and covariates are defined, the key concept of a "nearest neighbor" can be put forth. Given the state x_k and a certain covariate p, the N nearest-neighbor states (denoted as $\{x_k^j\}_{j=1}^N = \mathrm{NN}(x_k, p)$) are defined as the states x that are closest to x_k in the database and which share the same covariate vector p. Here, a measure of "closeness" is conveniently defined in terms of the quadratic distance between the state and its neighbors,

$$d(x, x_k) \equiv (x_k - x)^T W (x_k - x) \tag{5}$$

where w is an appropriately chosen weighting matrix.

5. Performance Measure

The performance measure is the probability of survival. For a patient in a given state x with covariate vector p, the survival probability is denoted by $S(x, p)$. It is evaluated simply by extracting the N nearest neighbor states to x of patients with the same covariate vector p and by noting the fraction of them that survived. For example, if N_s of the N nearest-neighbor states to x survived, then the survival probability is given as,

$$S(x, p) = \frac{N_s}{N} \tag{6}$$

6. Applications

6.1 Data mining

One can now trace through individual patient histories in the database and compute the associated probability of survival $S(x, p)$ as a function of time. A large change, either up or down, indicates a potentially significant role of the associated therapeutic modality, and its underlying physiologic mechanisms. The entire database can be mined for therapeutic modalities having the most efficacy or harm under specific conditions using this technique.

6.2. Real-Time Diagnostic Tool

The stochastic analysis is not restricted to subjects contained within the database. It can also be used on any real patient during his/her clinical care. In this case, the survival probability $S(x,u)$ is computed by tracking the subject's nearest neighbors in the database and providing to the clinician a real-time feedback signal which indicates the condition of the patient as a function of time, and the efficacy of any therapeutic modalities administered, or to be considered at that time.

6.3. Stochastic Control Optimal Therapy

By classifying a subject's nearest neighbors by the therapeutic modalities employed, the survival probabilities $P(u_i, x_k, p)$ can be computed separately for each modality u_i. A useful method for stochastic control then follows by administering the therapy associated with the highest value of $P(u_i, x_k, p)$. Intuitively, this therapeutic modality is optimal (and a worthwhile choice in practice) in the sense that it has the highest survival probability among the patient's nearest neighbors in the database.

The stochastic analysis and control approach is summarized in Figure 1. Examples of the second application above (i.e., use as a real-time diagnostic tool) will be given in the next section.

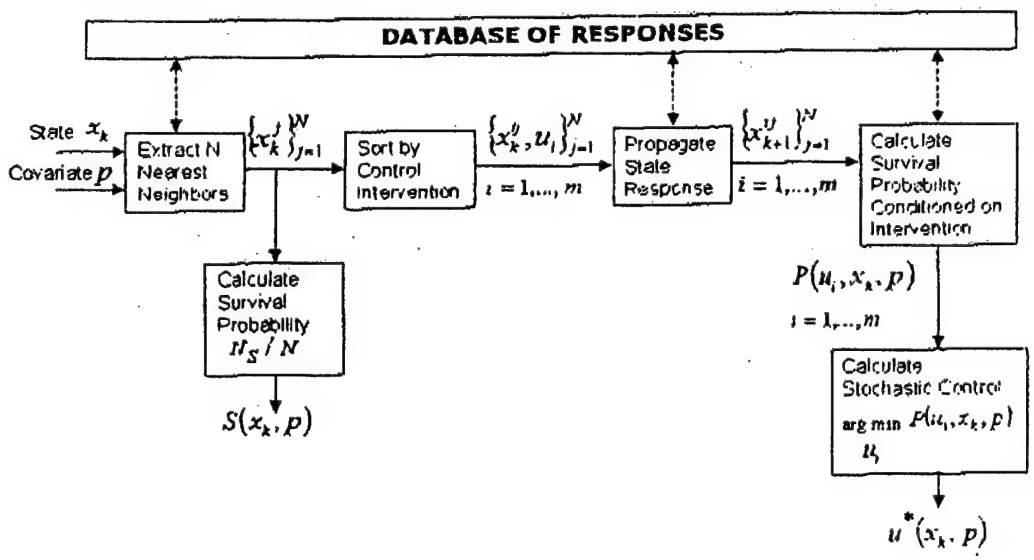

Figure1. Stochastic analysis and control synthesized using a database of responses.

7. Examples

In this section, two examples are given demonstrating the use of the stochastic analysis tool for real-time diagnosis. For this purpose, a hemodynamic database of responses is developed from the records of 316 acutely ill patients [5].

The covariate associated with truncal injury is chosen. The state is chosen as a vector whose elements are composed of the time t elapsed since admission, and observations $y_l, l = 1,....,7$ and their first and second derivatives y_l, y_l, and first integral $\int y_l du$ for each of the following observations: CI (cardiac index); HR (heart rate), MAP (mean arterial pressure), pulse oximetry arterial oxygen saturation $SapO_2$), transcutaneous oxygen $PtcO_2$; transcutaeneous carbon dioxide $PtcCO_2$; and HCT (hematocrit). The resulting state has 29 dimensions.

Data sets of two patients were removed from the database and treated as new patients. The probability of survival (bottom traces) is calculated using the stochastic analysis approach and plotted as a function of time in Figure 2 for patient 1 and in Figure 3 for patient 2.

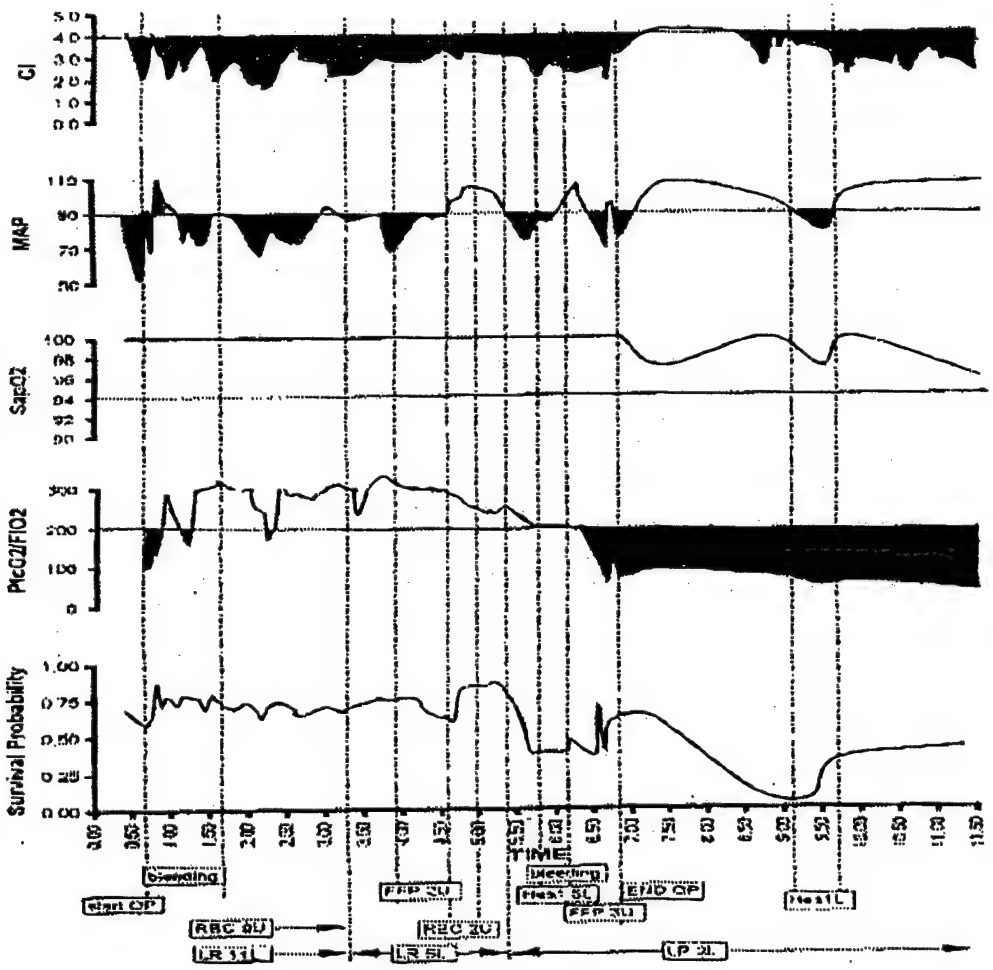

Figure2. Patient 1 Data - Upper row: Cardiac output (CI); Second Row: Mean arterial pressure (MAP); Third row: Pulse oximetry (SapO2); Fourth row: Transcutaneous FIO2 ratio; Lowest row: Survival Probability computed for this patient by the stochastic analysis and control program.

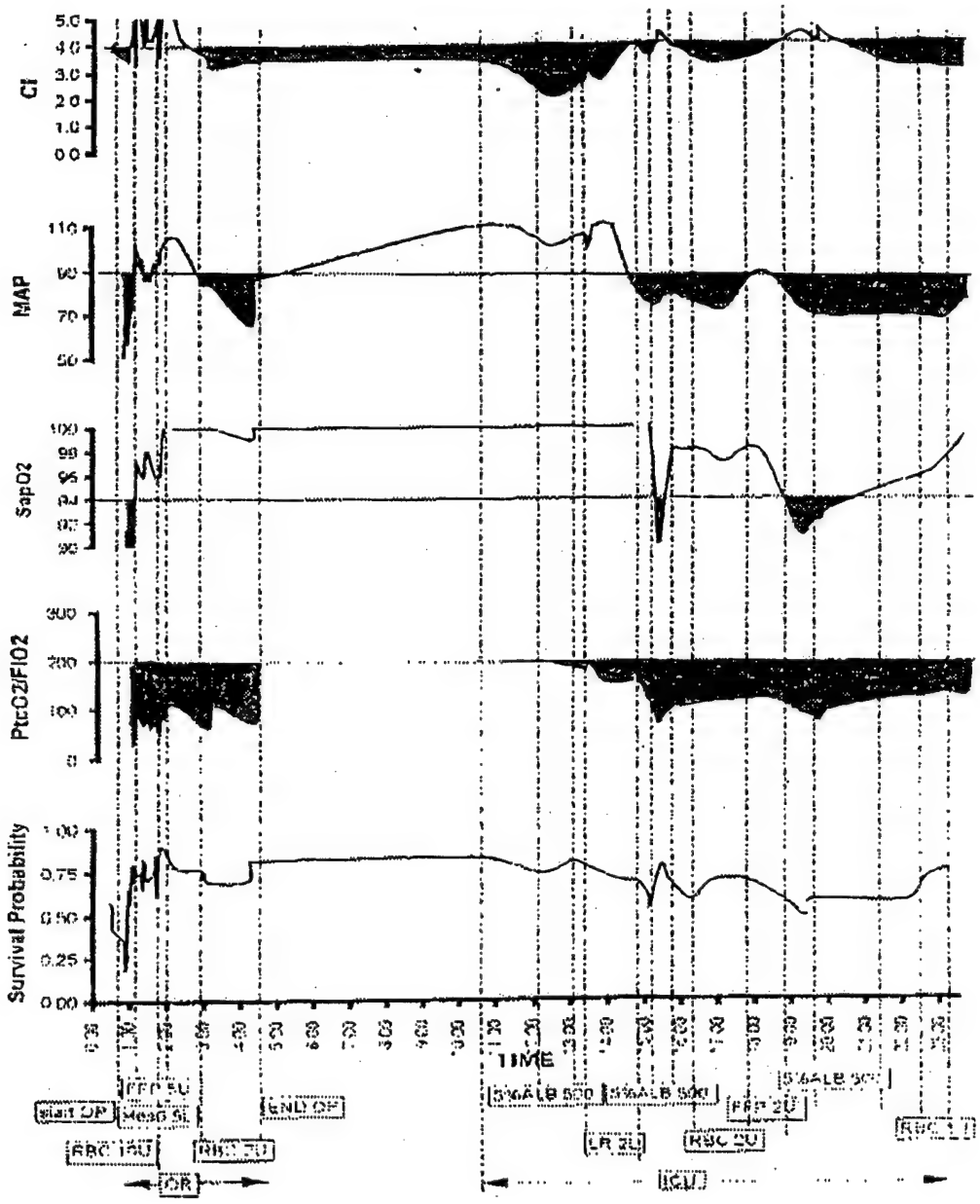

Figure 3 Patient 2 Data - Upper row: Cardiac output (CI); Second Row: Mean arterial pressure (MAP); Third row: Pulse oximetry (SapO2); Fourth row: Transcutaneous FIO2 ratio; Lowest row: Survival Probability computed for this patient by the stochastic analysis and control program)

In each figure, the dark areas are regions of deficit, where the patients' measurements fell below set thresholds into non-ideal territory. The more time spent in such regions (i.e., building up an "integrated deficit"), the more reason for concern for the well-being of the patient. This integrated deficit statistic has been studied separately and has emerged as a strong indicator of patient survivability in earlier studies [6]. It is used here to compare with the new survival

probability statistic. In each figure, time in hours from ED admission are noted on the dark horizontal line below the survival probability row. The start and end of the surgical operation (OP) are noted. Each therapy is noted in the oblong boxes, and times of the beginning and end of each therapy are noted by the vertical dotted lines.

In the data of patient 1, (Figure 2) continuing deficits in CI and the transcutaneous O^2/FIO^2 ratio resulted in a progressive lowering of this patient's survival probability beginning 5 hours after admission. The patient subsequently died on the 9th postop day. The survival probability correctly indicates this degrading trend, becoming smaller with time and ending with a survival probability of less than 50%.

In the data of patient 2 (Figure 3) there are relatively small deficits in CI values, which were usually above the normal value of 3 L/min/m^2, but not at the optimal values of 4 L/min/m^2. There was also slight hypotension, despite a relatively normal CI and the relatively low tissue perfusion indicated by the $PtcO^2/FIO^2$. Despite these mild to moderate deficiencies, this patient survived. The survival probability correctly predicts this optimistic trend. Following an initial low it remained above 75% toward the middle and at the end.

In both examples, it is seen that the survival probability has provided a reliable real-time diagnostic signal to indicate the condition of the patient.

8. Acknowledgements:

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Outcome Prediction of Emergency Patients by Noninvasive Hemodynamic Monitoring*

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Objectives: **We used noninvasive hemodynamic monitoring in the initial resuscitation beginning in the emergency department (ED) for the following reasons: (1) to describe early survivor and nonsurvivor patterns of emergency patients in terms of cardiac, pulmonary, and tissue perfusion deficiencies; (2) to measure quantitatively the net cumulative amount of deficit or excess of the monitored functions that correlate with survival or death; and (3) to explore the use of discriminant analysis to predict outcome and evaluate the biological significance of monitored deficits.**

Methods: **This is a descriptive study of the feasibility of noninvasive monitoring of patients with acute emergency conditions in the ED to evaluate and quantify hemodynamic deficits as early as possible. The noninvasive monitoring systems consisted of a bioimpedance method for estimating cardiac output together with pulse oximetry to reflect pulmonary function, transcutaneous oxygen tension to reflect tissue perfusion, and BP to reflect the overall circulatory status. These continuously monitored noninvasive measurements were used to prospectively evaluate circulatory patterns in 151 consecutively monitored severely injured patients beginning with admission to the ED in a university-run county hospital. The net cumulative deficit or excess of each monitored parameter was calculated as the cumulative difference from the normal value vs the time-integrated monitored curve for each patient. The deficits of cardiac, pulmonary, and tissue perfusion functions were analyzed in relation to outcome by discriminant analysis and were cross-validated.**

Results: **The mean (± SEM) net cumulative excesses (+) or deficits (−) from normal in surviving vs nonsurviving patients, respectively, were as follows: cardiac index (CI), +81 ± 52 vs −232 ± 138 L/m^2 ($p = 0.037$); arterial hemoglobin saturation, −1 ± 0.3 vs −8 ± 2.6%/h ($p = 0.006$); and tissue perfusion, +313 ± 88 vs −793 ± 175, mm Hg/h ($p = 0.001$). The cumulative mean arterial BP deficit for survivors was −10 ± 13 mm Hg/h, and for nonsurvivors it was −57 ± 24 mm Hg/h ($p = 0.078$).**

Conclusions: **Noninvasive monitoring systems provided continuously monitored on-line displays of data in the early postadmission period from the ED to the operating room and to the ICU for early recognition of circulatory dysfunction in short-term emergency conditions. Survival was predicted by discriminant analysis models based on the quantitative assessment of the net cumulative deficits of CI, arterial hypoxemia, and tissue perfusion, which were significantly greater in the nonsurvivors.**

(CHEST 2001; 120:528–537)

Key words: hemodynamic monitoring; multicomponent noninvasive circulatory monitoring; outcome prediction; pulse oximetry; temporal hemodynamic patterns; transcutaneous oxygen tension

Abbreviations: CI = cardiac index; ED = emergency department; FIO_2 = fraction of inspired oxygen; GCS = Glasgow coma scale; MAP = mean arterial BP; OR = operating room; PAC = pulmonary artery catheter; SaO_2 = arterial oxygen saturation; $tcPO_2$ = transcutaneous oxygen tension

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Hemodynamic bedside monitoring by pulmonary artery catheters (PACs) has been considered by many as the "gold standard" for critically ill patients, but its usefulness has been challenged,[1–7] particularly in the late stages of illness after the onset of

For editorial comment see page 339

organ failures. A meta-analysis by Boyd and Hayes[8] showed no outcome improvements in seven randomized studies of patients who entered the ICU after organ failure or sepsis had occurred, but there was significantly improved outcome in six other randomized studies, plus two more recent studies,[9,10] when PAC-directed therapy was given early or prophylactically. Since time may be important in the initial resuscitation and management of emergency patients, noninvasive monitoring is proposed as an alternative approach to identify and correct hemodynamic deficiencies at the earliest possible time. Previous studies have documented satisfactory correlation between thermodilution and bioimpedance cardiac output values for trauma patients in the emergency department (ED), the operating room (OR), and the ICU. The mean (± SEM) bias and precision in the ED were −0.058 ± 0.78 L/min/m^2.[11]

In the present study, we monitored severely injured emergency patients, beginning in the ED and continuing in the radiology department, the OR, and then in the ICU. Acute injury was studied because time factors are important and the time course of circulatory events could be monitored from the time of hospital admission.[11,12] Continuous visual displays of monitored data were used to evaluate rapidly changing patterns during unstable emergency conditions. Second, we time-integrated the differences between the monitored curve and normal values or reference values reflecting "optimal" goals derived from the patterns observed throughout the time course of previous series of survivors of acute severe illnesses or operations.[13–21] We then calculated the net cumulative excesses or deficits of each monitored variable for each patient and for the survivors and nonsurvivors. Finally, we explored the use of discriminant analysis to predict outcome based on these calculated cumulative deficits.

Materials and Methods

Clinical Series

We satisfactorily studied 151 of 155 consecutively monitored major trauma patients with noninvasive circulatory monitoring beginning shortly after their admission to the ED and continuing into the radiology department, the OR, through the postanesthesia recovery area, and to the ICU. Four patients were excluded because of insufficient data due to technical equipment failure or communication issues with personnel; the present report describes the data of 151 patients. Table 1 lists the salient clinical features of the series. Patients with major blunt trauma or penetrating trauma and significant risk of mortality or morbidity were selected for monitoring prior to possible emergency surgery. The criteria for resuscitation were empirically determined by the previous series of survivors' values and by the best possible initial responses of the cardiac index (CI) and the other hemodynamic variables.[12–14] Monitoring was continued until a plateau was reached after vigorous fluid and inotropic therapy resuscitation or until 24 h had elapsed. Optimal hemodynamic goals were sought, in so far as possible, but the adequacy of initial resuscitations may have been limited in part by clinical exigencies at the time. The calculation of cumulative excesses or deficits and discriminant analysis were performed after monitoring was completed. The institutional review board approved the protocol.

Table 1—*Clinical Features

Variables	Survivors (n = 103)	Nonsurvivors (n = 48)	p Value†
Age, yr	35 ± 4	40 ± 3	0.25
Gender			
Male	90 (87)	41/48 (85)	0.937
Female	13 (13)	7/48 (15)	0.937
Mechanism of injury			
Gunshot wound	42/61 (69)	19/61 (31)	0.001
Blunt trauma	41/68 (60)	27/68 (40)	0.03
Stab wound	20/22 (91)	2/22 (9)	0.001
Bodily injury			
Head	24/41 (59)	17/41 (41)	0.159
Chest	50/68 (73)	18/68 (26)	0.001
Abdomen	54/84 (64)	30/84 (36)	0.001
GCS	13.3 ± 0.3	9.4 ± 0.7	0.001
Injury severity score	21.8 ± 4.7	30.5 ± 4.6	0.24

*Values given as No. (%) or mean ± SD.
†p Values for differences between the number and percentages of survivors vs nonsurvivors.

Mean Arterial BP

Continuous mean arterial BP (MAP) was measured noninvasively (Dynamap system; Criticon; Tampa, FL) or was calculated electronically from transducers in line with intra-arterial catheters when the latter were used.

Cardiac Output

A thoracic bioelectric impedance device (IQ system; Wantagh Inc; Bristol, PA) was applied shortly after the arrival of the patient in the ED. Pairs of noninvasive, disposable, prewired hydrogen electrodes were positioned with one pair placed on each side of the base of the neck and two other pairs placed one on each side of the chest at the level of the zyphisternal junction opposite the lateral axillary line. Three ECG leads were placed across the precordium and left shoulder.[22,23] A 100-KHz, 4-mA alternating current was passed through the patient's thorax by the outer pairs of electrodes, and the voltage was sensed by the inner pairs of electrodes; the voltage sensed by the inner electrodes captured the baseline impedance, the first derivative of the impedance waveform, and the ECG. The ECG and bioimpedance signals were filtered with an all-integer-coefficient technology to decrease computation and signal-processing times. The signal-processing algorithm used a time-frequency distribution (modified Wigner distribution) analysis that increased signal-to-noise ratios.[22,23] The data were automatically acquired and downloaded to a floppy disk. When indicated by clinical criteria, PACs were inserted into the patient in the OR or the ICU, and CI estimations were made at least hourly in unstable patients and every 4 h in stable patients. The optimal goal for CI in various etiologic diagnostic groups was defined by survivors' values[12–14] and was tested in subsequent studies.[14–21]

Limitations of the impedance method include faulty electrode placement, motion artifacts, restlessness, shivering, pulmonary edema, pleural effusion, valvular heart disease, dysrhythmias, and electrical leaks from other instruments using the same circuit. These are usually apparent from inspection of the impedance waveform and by the following previously described criteria: baseline impedance > 15 ohms and impedance signal > 0.3 ohm, which usually indicate pulmonary edema due to cardiac failure or late-stage ARDS.[11] These limitations were excluded during the time of monitoring in the present study.

Pulse Oximetry

Arterial oxygen saturation (Sa_{O_2}) was assessed continuously by pulse oximetry (Nellcor; Pleasanton, CA) as a reflection of pulmonary gas exchange. Values were observed and recorded at the time of the CI measurements. Appreciable or sudden changes in these values also were noted, and changes to < 94% were confirmed by Sa_{O_2} measurement obtained by standard blood gas analysis.[11,12]

Transcutaneous Oxygen Tension

Standard transcutaneous oxygen tension ($tcPo_2$) measurements were continuously monitored throughout the observation period. This technology uses the same Clark polarographic oxygen electrode routinely employed in standard blood gas measurements.[24–30] The oxygen tensions were measured in a representative area of the skin surface heated to 4°C to increase diffusion of oxygen across the stratum corneum and to avoid vasoconstriction in the local area of the skin being measured.[27] Previous studies demonstrated the capacity of transcutaneous oxygen tensions to reflect tissue oxygen tension.[11,12,25,28] $tcPo_2$ has been shown to reflect the delivery of oxygen to the local area of skin; it also parallels the mixed venous oxygen tension except under late or terminal conditions in which peripheral shunting leads to high mixed venous hemoglobin saturation values.[24] While oxygen tension of a segment of the skin does not reflect the state of oxygenation of all tissues and organs, the skin has the advantage of being the most sensitive early warning tissue of the adrenomedullary stress response; vasoconstriction of the skin is an early stress response to hypovolemia and other shock syndromes.[11,12,24] $tcPo_2$ Values were indexed to the fraction of inspired oxygen (Fio_2) concentration to give a $tcPo_2/Fio_2$ ratio because of marked $tcPo_2$ changes produced by changes in the level of inspired oxygen. The thermal environment was maintained at reasonably constant levels, and marked changes in room temperature from drafts or open windows were avoided to maintain the accuracy of the transcutaneous methods. In addition, the electrode must be moved to a nearby thoracic or shoulder site every 4 h and recalibrated to avoid first-degree skin burns.

Level of Consciousness

At the time of the patient's admission to the ED, the clinical team evaluated and recorded the degree of unconsciousness by the Glasgow coma scale (GCS), which uses eye movement, verbal responses, and motor responses to verbal and painful stimuli. The clinical service also noted changes in the GCS throughout the patient's hospital course.

Estimated Blood Loss at the Time of Surgery

Blood loss was estimated by the surgeon and anesthesiologist intraoperatively in a routine manner by counting lap tapes and sponges and by measuring the contents of suction bottles.

Method for Calculating the Total Cumulative Excess or Deficit of Each Monitored Variable

The patterns of each patient were examined for motion artifact, noise, effects of fluid and vasopressor therapy, manipulation of tubing, and other extraneous factors. The total overall deficit or excess of each noninvasively monitored variable was evaluated by comparing its normal or optimal value with its temporal pattern during the observation period. This was done by mathematically integrating over time the area between the continuous display of each fluctuating variable and either the normal values for BP, Sa_{O_2}, and $tcPo_2/Fio_2$ or the optimal goal, as defined by the CI values of survivors during the first 24 h after hospital admission.[11–21]

The net cumulative deficits or excesses were calculated for each individual patient and for both survivor and nonsurvivor groups as time-integrated areas between the curve produced by continuously monitored variables and their normal or reference values. For example, given a normal MAP of 85 mm Hg, in a patient whose MAP averaged 60 mm Hg for 2 h before resuscitation, the calculated deficit is −50 mm Hg/h ([85–60] × 2).

Flow calculations, measured as volume per unit of time, are in liters per minute per square meter. When multiplied by the monitored time in minutes, this gives, as units, liters per square meter for CI or liters for cardiac output. The units for MAP, Sa_{O_2}, and $tcPo_2/Fio_2$ are millimeters of mercury per hour, percent per hour, and millimeters of mercury per hour, respectively.

When the mean MAP deficits were calculated using all values, a large number of normal high values obscured the deficits; the patients with cardiac arrest and zero MAP, for example, showed no net MAP deficit, because the many normal and high values overshadowed the later short but lethal hypotensive episode. For MAP, therefore, we calculated cumulative deficits from decreases below the normal range.

Statistical Analysis

The survivors' and nonsurvivors' deficits of MAP, CI, Sa_{O_2}, and $tcPo_2/Fio_2$ were calculated for the periods of monitoring. Each of the categoric variables was tested for the difference in distributions between the two outcome groups, those who survived and those who died during the current hospitalization, using the χ^2 test or two-tailed Fisher's Exact Test. The t test with Bonferroni correction was applied to each of the continuous variables to compare the means of the two outcome groups. Variables considered for discriminant analysis were CI, GCS, Sa_{O_2}, $tcPo_2/Fio_2$, MAP, heart rate, Pa_{O_2}, hematocrit, transcutaneous CO_2 tension ($PtcCO_2$), injury severity score, age, and gender. The first four met the criteria ($p < 0.20$).

The variables that were significant at the $p < 0.2$ level by the aforementioned χ^2 tests or the t tests were fed into a stepwise discriminant analysis (PROC STEPdisk) to identify the variables that collectively contribute to differentiate the two outcome groups. Thus, the variables selected then were entered into a model in PROC DISCRIM to derive the discriminant function by generalized squared distance, taking into account the prior probabilities of the groups. This procedure evaluated the discriminant function by calculating the error rate estimates or the probabilities of misclassification.

Cross-validation of the results was performed by the jackknife method. The data were split into two independent samples by taking the data of every other patient. One group was used for calibration to generate another series of classification functions, and the remaining group was used to calculate results based on the new classification functions. The statistical analyses were performed with a computer program (SAS for Windows, Release 6.12; SAS Institute; Cary, NC).

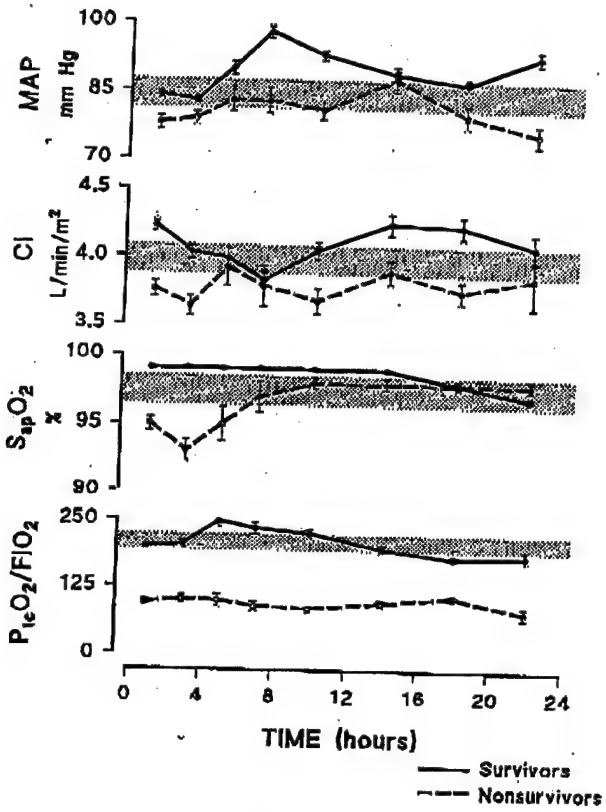

FIGURE 1. The temporal patterns of survivors (solid line) and nonsurvivors (dashed line) for MAP, CI, SaO_2 ($SapO_2$), and $tcPO_2$ ($PtcO_2$) indexed to the $tcPO_2/FIO_2$ ratio. All values are keyed to the time of admission to the ED. Dots represent mean values, and vertical lines represent SEM. Cross-hatched areas indicate the normal range for MAP, Sao_2, and $tcPO_2/FIO_2$ ratio and optimal goals for CI. Note that the CI, MAP, Sao_2, and $tcPO_2/FIO_2$ values of survivors were generally higher than those of the nonsurvivors.

RESULTS

Noninvasive Monitoring From the Time of Admission

The use of noninvasive monitoring systems was found to be feasible in patients experiencing short-term emergency conditions for the early description of temporal hemodynamic patterns and to provide quantitative calculations of the total amount of deficit or excess accumulated by each monitored variable. There were 103 survivors and 48 nonsurvivors (mortality rate, 32%), 131 patients were men, 20 patients were women, and the average (± SEM) age was 35 ± 1.4 years. Of 61 patients with gunshot wounds, 42 survived and 19 died (mortality rate, 31%). Of 68 patients with blunt trauma, 41 survived and 27 died (mortality rate, 40%). Of 22 patients who sustained stab wounds, 20 survived and 2 died (mortality rate, 9%). Of 41 patients who had head injuries, 24 survived and 17 died (mortality rate, 41%). Of 68 patients who sustained chest injuries, 50 survived and 18 died (mortality rate, 26%). Of 84 patients who sustained abdominal injuries, 54 survived and 30 died (mortality rate, 36%). Sixty-eight patients had injuries involving more than one bodily area. The injury severity score (± SEM) was 21.8 ± 4.7 for survivors and 30.5 ± 4.6 for nonsurvivors ($p = 0.24$).

Monitoring was performed for 7.9 ± 2.6 h during the initial resuscitation (survivors, 7.8 h; nonsurvivors, 8.3 h). Subsequently, survivors were monitored intermittently to 15.6 ± 7.1 h after hospital admission, and nonsurvivors were monitored to 18.7 ± 8.4 h after hospital admission.

The data of emergency patients from the time of their ED admission are shown in Figure 1. The correlation between simultaneous thermodilution and bioimpedance cardiac output measurements in the present series was $r = 0.91$ and $r^2 = 0.83$, and bias and precision were -0.30 ± 1.10 L/min/m^2. Table 2 lists the mean ± SEM of CI, MAP, Sao_2, and $tcPO_2/FIO_2$ for survivors and nonsurvivors averaged throughout the observation period. The CI, Sao_2, and $tcPO_2/FIO_2$ values of patients who survived were significantly greater than for those who died. MAP values of survivors tended to be higher than those for nonsurvivors ($p = 0.066$) (Table 2).

The body temperatures of survivors and nonsurvivors at hospital admission averaged 36.7 ± 0.0°C to 7°C and 36.3 ± 0.0°C to 9°C, respectively. We took aggressive precautions to correct hypothermia when it occurred, especially in the OR where conditions were more controllable.

Table 2—*Noninvasive Hemodynamic Values for Survivors and Nonsurvivors**

Variable	Normal or Optimal Value	Survivors (n = 103)	Nonsurvivors (n = 48)	p Value†
CI, L/min/m²	4.0	4.14 ± 0.02	3.87 ± 0.03	< 0.001
MAP, mm Hg	85	88 ± 0.37	80 ± 0.69	0.066
Sao_2, %	98	99 ± 0.05	96 ± 0.26	< 0.001
$tcPO_2/FIO_2$, mm Hg	200	206 ± 2.9	93 ± 2.6	< 0.001

*Values given as mean ± SEM, unless otherwise indicated.
†p Values for differences between survivors' and nonsurvivors' values.

Table 3—*Time to Reach Goal in Patients Who Attained Goal**

Variable	Survivors		Nonsurvivors	
	Hours	No./% Goals Not Reached	Hours	No./% Goals Not Reached
CI	1.99 ± 5.10	6/6	2.64 ± 3.69	13/28
MAP	1.34 ± 2.80	0/0	2.03 ± 3.69	16/34
Sao_2	0.48 ± 1.66	0/0	1.86 ± 4.44	9/19
$tcPo_2/Fio_2$	3.14 ± 4.61	7/7	4.48 ± 4.56	39/83

*Values given as mean ± SD, unless otherwise indicated.

The mean (± SD) estimated blood loss, which reflects preoperative and intraoperative hemorrhaging, measured 2,970 ± 3,856 mL in survivors and 6,263 ± 5,540 mL in the nonsurvivors at the end of surgery. In the present series, there were 22 patients who had massive blood loss (*ie*, > 5,000 mL). Vigorous attempts were made to replace these losses at the time of surgery and in the immediate postoperative period.

Temporal Circulatory Patterns in Survivors and Nonsurvivors

Figure 1 shows the temporal patterns of noninvasive circulatory variables of the survivors and nonsurvivors beginning with the initial measurements after admission to the ED. CI values were initially higher in the survivors. The Sao_2 values of nonsurvivors were significantly lower than the those of survivors, but these differences were not clinically important; when Sao_2 reductions occurred, they were rapidly corrected by intubation, mechanical ventilation, or increased Fio_2. The values for the $tcPo_2/Fio_2$ ratios of nonsurvivors were markedly lower than those of survivors and were lower than normal throughout the observation period. Table 3 lists the time taken to achieve goals of therapy for each variable that reached the desired end point as well as the number and percentage of those who did not reach the goals. The deaths of nonsurvivors occurred an average of 8.7 ± 2.8 days after hospital admission. However, there was a bimodal distribution with 17 deaths in the first 8 h and 14 deaths occurring ≥ 10 days after hospital admission.

Net Cumulative Amount of Deficit or Excess in Monitored Variables

Table 4 shows the net cumulative deficit or excess of monitored variables used to evaluate cardiac, pulmonary, and tissue perfusion functions. Figure 2 is an illustrative example of a survivor whose CI and tissue perfusion deficiencies were corrected at 19 and 23 h postadmission, respectively. Figure 3 shows the data of a patient whose CI and tissue perfusion deficiencies persisted for > 24 h. He developed lethal ARDS.

Outcome Prediction

There were significantly greater calculated deficits of CI, pulse oximetry, and transcutaneous O_2 in nonsurvivors than in survivors during the period of monitoring (Fig 4 and Table 4). These three variables and the GCS, having moderate levels of significance with outcome, were selected for the stepwise discriminant analysis (PROC STEPdisk). Based on the classification function generated for each of these four variables in PROC DISCRIM, the discriminant function, Z, was derived:

$$Z = 0.0011a + 0.3300b + 0.0656c + 0.0423d$$

where *a* represents cumulative $tcPo_2/Fio_2$ values, *b*

Table 4—*Mean Net Cumulative Deficits or Excesses of Monitored Values of Survivors and Nonsurvivors Throughout the Period of Observation*

Variable	Survivors		Nonsurvivors		p Value*
	Mean	SEM	Mean	SEM	
CI, L/m^2	+ 81	52	− 232	138	< 0.007
MAP, mm Hg/h	− 10	13	− 57	24	0.078
Sao_2, %/h	− 1	0.3	− 8	2.6	< 0.006
$tcPo_2/Fio_2$, mm Hg/h	+ 313	87	− 793	175	< 0.001

*p Values are for differences between survivors' and nonsurvivors' values.

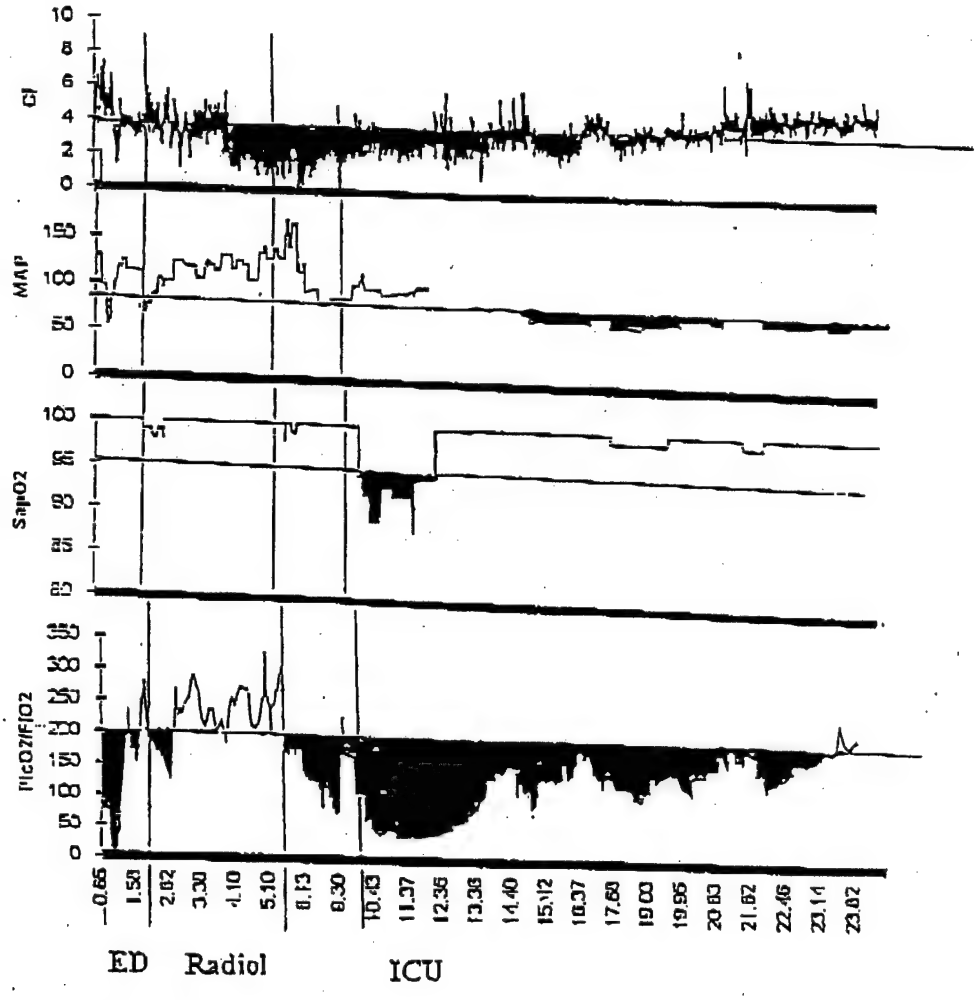

FIGURE 2. Data of a 64-year-old man who was hit by a car and sustained fractures of the pelvis, open left femur, left tibia, and fibula, and dislocation of the knee. He was given 6 U packed RBCs and 5,000 mL crystalloids in the ED. In the angiographic suite, he was given 6 more units of packed RBCs, 5 U fresh frozen plasma, and 2,000 mL crystalloids. His CI values became optimal (*ie*, 4 L/min/m^2) by about 18 h, and his $tcPO_2/FIO_2$ values reach the normal range in 24 h. The patient lived. See the legend of Figure 1 for abbreviations not used in the text.

represents the GCS, *c* represents cumulative Sao_2 values, and *d* represents cumulative CI values. Table 5 summarizes the relative influence of each variable with respect to outcome. Ninety-five percent of the survivors and 62% of the nonsurvivors were correctly classified in the first 24 h postadmission (Table 6). Of 151 patients, 23 (15.2%) were misclassified. Five of the 35 patients predicted to die in the first 24 h subsequently improved and lived.

Results of Cross-Validation

Cross-validation of the discriminant analysis by the jackknife method demonstrated results that were similar to the initial calculation for the series as a whole. The results of the calibration data set (N = 75) are shown in Table 7, and the results from the validation data set (N = 76) are shown in Table 8. The cross-validated discriminant analysis was

$$Z + 0.0018a + 0.3138b + 0.0786c + 0.0022d$$

where *a*, *b*, *c*, and *d* are defined as above. The classification of the survivors was $Z > 1.91$. Miscalculations occurred in 12 of 76 patients (16%). This was considered to be in satisfactory agreement with the initial calculation and suggests consistency of the data by this analysis.

DISCUSSION

The limitations of noninvasive bioimpedance cardiac output monitoring include motion artifacts,

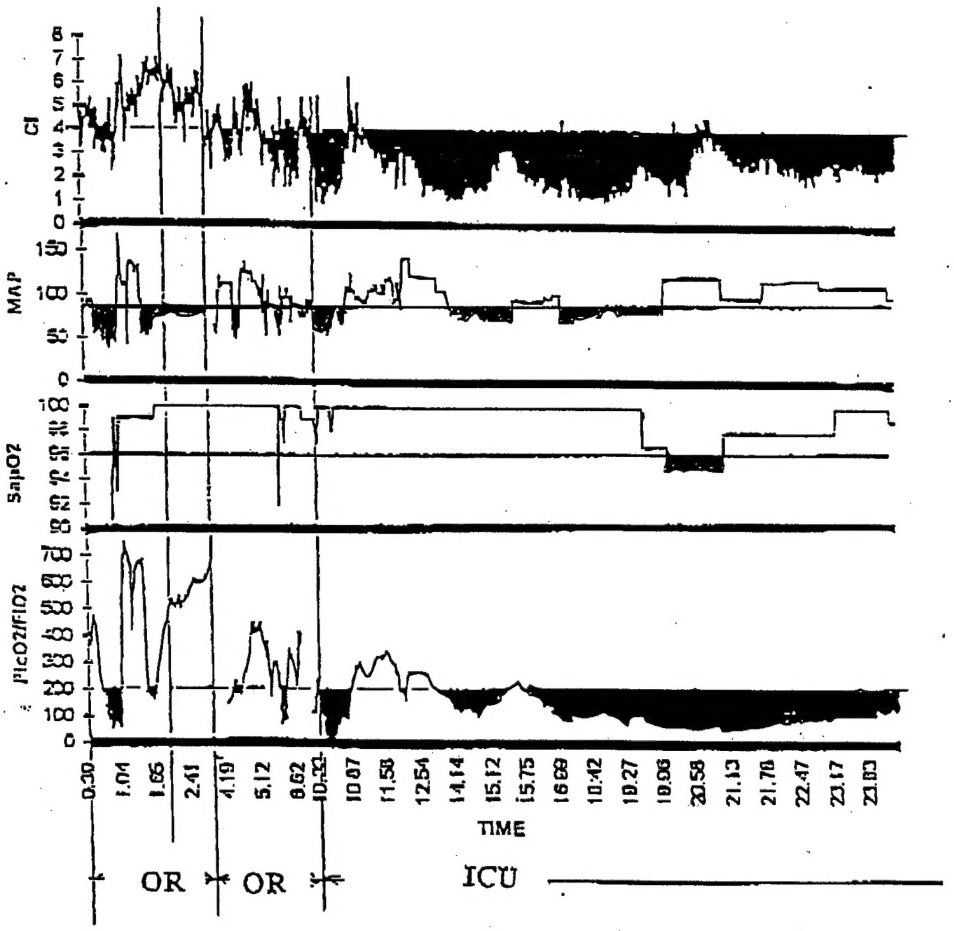

FIGURE 3. Data from a 26-year-old man who sustained multiple stab wounds of the abdomen with lacerations of the stomach, duodenum, and superior mesenteric vein. He had marked reduction of cardiac output and tissue perfusion despite the administration of 48 U packed RBCs, 5 U whole blood, 12,500 mL lactated Ringer's solution, 10 U platelets, 13 U fresh-frozen plasma, and 1,000 mL hetastarch, in addition to dobutamine and dopamine infusions for an estimated 18,000-mL blood loss. The patient died of ARDS and multiple organ failure. See the legend of Figure 1 for abbreviations not used in the text.

arrhythmias, pulmonary edema, pleural effusions, and expansion of interstitial fluid from massive crystalloid infusions. The advantages of this noninvasive monitoring system include technical convenience and the continuous display of data allowing the calculation of the amount of deficit or excess of each variable, from the time-integrated area under the curve. The area under the curve provides an arithmetic solution to replace the subjective evaluation of irregular curves and provides estimates of cardiac, pulmonary, and tissue perfusion functions.

Table 5—*Stepwise Discriminant Analysis**

Step Entered	Partial R^2	Prob > F	Cumulative R^2†
1. Cumulative $tcPo_2/FIo_2$	0.210	0.0001	0.2099
2. GCS	0.188	0.0001	0.3581
3. Cumulative SaO_2	0.053	0.0047	0.3921
4. Cumulative CI	0.031	0.0336	0.4107

*Classification of survivors, Z > 2.36; where Z = 0.0011 (cumulative $tcPo_2/F(o_2)$ + 0.3300 (GCS) + 0.0656 (cumulative SaO_2) + 0.0423 (cumulative CI).
†Pillai's trace/(No. of groups − 1).

Table 6—*Classification Summary for the Series (n = 151)**

Actual Outcome	Predicted to Die		Predicted to Live		Total	
	No.	Row%	No.	Row%	No.	Col%
Died	30	62.5	18	37.5	48	31.8
Lived	5	4.9	98	95.1	103	68.2
Total, %	35	23.2	116	76.8	151	100.0

*Misclassification: 23/151 (15.2%). Row% = the percentage of patients in that row; Col% = the percentage of patients in that column.

Table 7—*Classification From the Calibration Dataset (n = 75)**

Actual Outcome	Predicted to Die		Predicted to Live		Total	
	No.	Row%	No.	Row%	No.	Col%
Died	15	62.5	9	37.5	24	32.0
Lived	3	5.9	48	94.1	51	68.0
Total, %	18	24.0	57	76.0	75	100.0

*Misclassification: 12/75 (16.0%). See Table 6 for abbreviations not used in text.

Table 8—*Classification From the Validation Dataset (n = 76)**

Actual Outcome	Predicted to Die		Predicted to Live		Total	
	No.	Row%	No.	Row%	No.	Col%
Died	15	62.5	9	37.5	24	31.6
Lived	5	9.6	47	90.4	52	68.4
Total, %	20	26.3	56	73.7	76	100.0

*Misclassification: 14/76 (18%). See Table 6 for abbreviations not used in text.

The net cumulative deficits of flow and tissue perfusion measured during the initial resuscitation period were greater in nonsurvivors than survivors; these differences were correlated with outcome. For example, during the monitoring period, the CI values of survivors averaged 81 L/m^2 more than the optimal 4.0 $L/min/m^2$, which was determined empirically from the plateau of high values of survivors within the first 24 h of hospital admission.[11,21] This was equivalent to 140 L of cardiac output per patient over the monitored period. During the monitoring period of those who died, the CI averaged 232 L/m^2 less than optimal, and the cardiac output averaged 402 L per patient less than optimal. The difference between survivors and nonsurvivors was 542 L. We used 4.0 $L/min/m^2$ as the therapeutic goal because this was the mean value for the first 24-h period, on which this study was focused. This goal admittedly is arbitrary and points to the need for additional research in this area.

The high early CI values in survivors suggest that there may have been less hypovolemia and/or better physiologic compensations. This concept is reinforced by the greater $tcPO_2/FIO_2$ net cumulative excesses, which suggest better tissue perfusion/oxygenation for survivors in the initial stages. These preliminary studies need to be evaluated independently in larger series with different types of acute illnesses and emergency conditions. Furthermore, additional studies are needed to evaluate the effects of specific trunk and extremity traumas, head injuries, pelvic and long bone fractures, prior organ dysfunctions, and other comorbid states on the validity of this early predictive model.

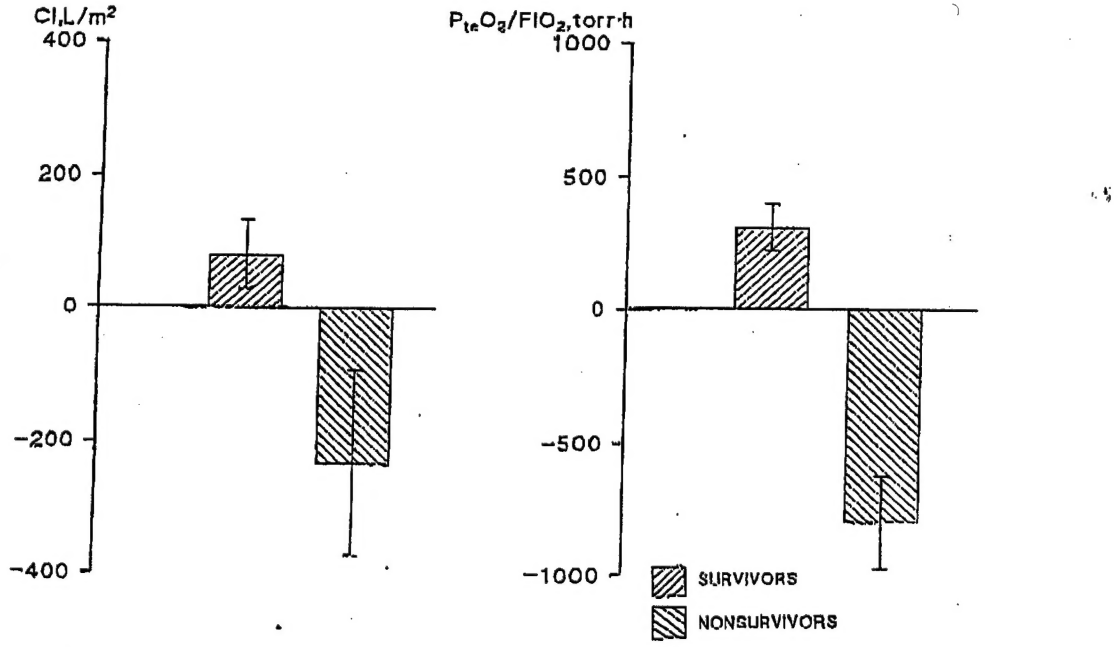

FIGURE 4. Cumulative excesses and deficits in survivors and nonsurvivors for CI and $tcPO_2/FIO_2$ calculated for the monitored period. See the legend of Figure 1 for abbreviations not used in the text.

The hypothesis underlying this approach is that circulatory deficiencies that ultimately lead to shock, organ failure, and death may be identified early by noninvasive monitoring even in the extenuating circumstances of severely traumatized emergency patients in a large inner city public hospital. Earlier diagnosis of a circulatory deficiency allows therapy to be initiated sooner in the hope that earlier therapy may improve outcome in emergencies where time is crucial.

More importantly, noninvasive monitoring, which has been reported to be easy, cheap, fast, safe, and sensitive,[11,12] allows estimates of the amount of deficits calculated from the difference in the areas between normal values or survivor values and the continuously monitored variables. Multiple noninvasive hemodynamic monitoring systems provide similar information to that of the PAC, except for pulmonary artery occlusion pressures. Discriminant analysis of these data provides a mathematical basis for outcome prediction. Future prospective clinical trials at other institutions are needed to validate the present approach.

Noninvasive monitoring also provides an approach that may be used to develop an organized coherent therapeutic plan based on physiologic criteria for the emergency patient as he/she proceeds from the ED to the OR, the radiology department, and the ICU. Linear discriminant function predicted outcome correctly in 95% of the survivors and in 62% of the nonsurvivors in the early period after hospital admission. This was probably as much as should be expected for nonsurvivors since many patients developed lethal complications unrelated to their injuries late in their hospital course.

Since the essence of tissue perfusion is an adequate supply of oxygenated blood to the tissues, perfusion is inferred from the direct measurement of skin oxygenation using the Clark polarographic method for oxygen tension.[24–29] Although the skin is not representative of all tissues, it is the largest organ and the first organ to be affected by the adrenomedullary stress response. $tcPo_2$ provides early warning in acutely ill emergency patients[11]; it tracks oxygen uptake in acute clinical shock episodes[11] and in the physiologic course of experimental hemorrhagic shock[24] as well as cardiac and respiratory failure, cardiac arrest, and cardiopulmonary resuscitation in acute surgical conditions.[28,30–36] As shown in the present study, this measure of tissue perfusion was related to outcome.

In the present study, we used discriminant analysis to analyze the data of variables with p values < 0.2 in order to limit the number of variables for analysis. Interrelated or poorly conditioned variables having a common term, such as the combination of CI and oxygen delivery, were avoided to minimize statistical problems of discriminant analysis. This does not mean that the more conventional variables like tachycardia, hypotension, acidosis, skin color, lactate levels, mental status, etc, are not useful at times when they occur. Obviously, when they are abnormal, they are extremely useful and important. However, the criteria of the present study focused on early noninvasive hemodynamic variables in the immediate postadmission period that most consistently separated survivors and nonsurvivors.

The concept that hypovolemia is an early primary problem that plays an important role in low flow and poor tissue perfusion states is supported by the following: (1) direct observation of massive hemorrhage; (2) estimated blood loss of hemoperitoneum and hemothorax at the time of surgery in patients who underwent surgical exploration; and (3) prior studies in the literature that documented blood volume deficits in posttraumatic and postoperative patients who subsequently developed organ failures and died.[37]

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